GenCore version 5.1.6

OM protein - protein search, using sw model

Run on: January 21, 2004, 09:14:54 ; Search time 2.1109 Seconds
(without alignments)
601.551 Million cell updates/sec

Title: US-09-869-414A-67
Perfect score: 40
Sequence: 1 EVKMDAEF 8

Scoring table: BLOSUM62
Gapop 10.0 , Gapext 0.5

Searched: 1107863 seqs, 158726573 residues

Total number of hits satisfying chosen parameters: 1107863

Minimum DB seq length: 0
Maximum DB seq length: 2000000000

Post-processing: Minimum Match 0%
Maximum Match 100%
Listing first 45 summaries

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Pred. No. is the number of results predicted by chance to have a
score greater than or equal to the score of the result being printed,

and is derived by analysis of the total score distribution.

SUMMARIES

Result No.	Score	% Query Match	Length	DB	ID	Description
1	40	100.0	8	21	AAY94772	Beta-secretase sub
2	40	100.0	8	22	AAE10660	Human Aspartyl pro
3	40	100.0	8	22	AAE06902	Human amyloid prec
4	40	100.0	8	22	AAU06631	Beta secretase sub
5	40	100.0	8	22	AAU06635	Synthetic fluoresc
6	40	100.0	8	22	AAU07230	Human beta-amyloid
7	40	100.0	8	22	AAE02612	Human Aspartyl pro
8	40	100.0	8	23	ABB78621	APP Swedish mutant
9	40	100.0	9	19	AAW82083	Fluorogenic protea
10	40	100.0	9	21	AAB07873	A peptide fragment
11	40	100.0	9	21	AAY87949	Mammalian amyloid
12	40	100.0	9	23	ABU60430	Protease binding p
13	40	100.0	10	13	AAR22054	Peptide P1. Synth
14	40	100.0	10	13	AAR24261	Human amyloidin pr
15	40	100.0	10	20	AAW82440	Human amyloid beta
16	40	100.0	10	21	AAY69703	Beta-APP alpha-sec
17	40	100.0	10	22	AAE10654	Human wild-type AP
18	40	100.0	10	22	AAE06899	Human amyloid prec
19	40	100.0	10	22	AAU06628	Asp2 recognition s
20	40	100.0	10	22	AAU07227	Human beta-amyloid
21	40	100.0	10	22	AAG62668	Beta-sheet breaker
22	40	100.0	10	22	AAE02606	Human wild-type AP
23	40	100.0	10	22	AAB66574	Synthetic peptide
24	40	100.0	10	22	AAB46207	Human APP derived
25	40	100.0	10	22	AAB46208	Human APP derived
26	40	100.0	10	22	AAB46209	Human APP derived
27	40	100.0	10	22	AAB61336	Sythetic peptide f
28	40	100.0	10	23	ABG78375	Human beta amyloid
29	40	100.0	10	23	ABG30940	Nogo/BACE method c
30	40	100.0	10	23	AAU99490	Peptide #1 used as
31	40	100.0	10	23	ABB78615	Beta-secretase spe
32	40	100.0	10	23	ABB06426	Human APP beta-sec
33	40	100.0	10	24	ABG76103	Amyloid precursor
34	40	100.0	11	22	AAB75143	APP beta-secretase
35	40	100.0	11	22	AAB75144	Asp 1 substrate se
36	40	100.0	11	22	AAB97468	Asp2 substrate wil
37	40	100.0	12	22	AAB74931	Beta-amyloid precu
38	40	100.0	12	23	ABB08997	Amyloid precursor
39	40	100.0	12	23	ABB07592	Biotinylated synth
40	40	100.0	12	23	AAE16657	APP substrate pept
41	40	100.0	12	23	AAU74831	Synthetic amyloid
42	40	100.0	12	24	AAO26795	Beta-secretase sub
43	40	100.0	13	19	AAW70869	Beta-amyloid pepti
44	40	100.0	13	23	AAM50891	Fluorescent substr
45	40	100.0	13	24	ABP71624	Beta-secretase act

ALIGNMENTS

RESULT 1
AAY94772
ID AAY94772 standard; Protein; 8 AA.
XX
AC AAY94772;
XX
DT 12-FEB-2001 (first entry)
XX
DE Beta-secretase substrate peptide SEQ ID 18.
XX
KW Beta-secretase; enzyme; amyloid plaque; Alzheimer's disease;
KW Down's syndrome; amyloid angiopathy; gene therapy; neuroprotective.
XX
OS Synthetic.
XX
PN WO200058479-A1.
XX
PD 05-OCT-2000.
XX
PF 23-MAR-2000; 2000WO-US07755.
XX
PR 26-MAR-1999; 99US-0277229.
XX
PA (AMGE-) AMGEN INC.
XX
PI Citron M, Vassar RJ, Bennett BD;
XX
DR WPI; 2000-594643/56.
XX
PT Isolated beta-secretase nucleic acids and encoded polypeptides, useful
PT for diagnosis and gene therapy of Alzheimer's disease -
XX
PS Example 10; Page 117; 145pp; English.
XX
CC This invention relates to 3 nucleotide sequences encoding beta-secretase
CC proteins. Beta-secretase is an enzyme involved in the production of one
CC of the components of amyloid plaques involved in Alzheimer's disease. The
CC invention includes an expression vector comprising the nucleotide
CC sequence, a host cell comprising the expression vector, and a process for
CC producing the protein through culturing the transformed cells. Also
CC included in the invention are a polypeptide derivative of the
CC beta-secretase protein, a fusion protein comprising beta-secretase fused
CC to a heterologous amino acid sequence, and a method for modulating the
CC levels of beta-secretase polypeptide in a mammal comprising administering
CC the polynucleotide sequence. Beta-secretase exhibits neuroprotective and
CC nootropic activity. The beta-secretase nucleotide sequence may be used to
CC map locations of the beta-secretase gene and related genes on chromosomes
CC and as hybridization probes in diagnostic assays to test for the presence
CC of beta-secretase DNA or RNA, such as in Alzheimer's disease, Down's
CC syndrome, and amyloid angiopathy. The nucleotide sequence may also be
CC used as anti-sense inhibitors of beta-secretase expression, in gene
CC therapy of Alzheimer's disease, and for the identification of compounds
CC that modulate beta-secretase activity. Antibodies to the beta-secretase
CC protein may be used for in vitro and in vivo diagnostic purposes to
CC detect the presence of beta-secretase polypeptide in a body fluid or cell
CC sample. The present sequence represents a beta-secretase substrate
CC peptide.

XX
SQ Sequence 8 AA;

Query Match 100.0%; Score 40; DB 21; Length 8;
Best Local Similarity 100.0%; Pred. No. 9.3e+05;
Matches 8; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

```
Qy          1 EVKMDAEF 8
              ||||||||
Db          1 EVKMDAEF 8
```

RESULT 2
AAE10660
ID AAE10660 standard; peptide; 8 AA.
XX
AC AAE10660;
XX
DT 10-DEC-2001 (first entry)
XX
DE Human Aspartyl protease-1 (hu-Asp-1) beta-secretase, wild-type peptide.
XX
KW Human; aspartyl protease 1; Asp1; amyloid precursor protein; APP;
KW Alzheimer's disease; AD; dementia; neurofibrillary tangle; gliosis;
KW amyloid plaque; neuronal loss; proteolytic; nootropic; neuroprotective.
XX
OS Homo sapiens.
XX
FH Key Location/Qualifiers
FT Cleavage-site 4..5
XX
PN GB2357767-A.
XX
PD 04-JUL-2001.
XX
PF 22-SEP-2000; 2000GB-0023315.
XX
PR 23-SEP-1999; 99US-0155493.
PR 23-SEP-1999; 99US-0404133.
PR 23-SEP-1999; 99WO-US20881.
PR 13-OCT-1999; 99US-0416901.
PR 06-DEC-1999; 99US-0169232.
XX
PA (PHAA) PHARMACIA & UPJOHN CO.
XX
PI Bienkowkski MJ, Gurney M;
XX
DR WPI; 2001-444208/48.
XX
PT Polypeptide comprising fragments of human aspartyl protease with
PT amyloid precursor protein processing activity and alpha-secretase
PT activity, for identifying modulators useful in treating Alzheimer's
PT disease -
XX
PS Example 15; Page 92; 187pp; English.
XX
CC The patent discloses human aspartyl protease 1 (hu-Asp1) or modified

CC Asp1 proteins which lack transmembrane domain or amino terminal
CC domain or cytoplasmic domain and retains alpha-secretase activity
CC and amyloid protein precursor (APP) processing activity. The proteins
CC of the invention are useful for assaying hu-Asp1 alpha-secretase
CC activity, which in turn is useful for identifying modulators of
CC hu-Asp1 alpha-secretase activity, where modulators that increase
CC hu-Asp1 alpha-secretase activity are useful for treating Alzheimer's
CC disease (AD) which causes progressive dementia with consequent
CC formation of amyloid plaques, neurofibrillary tangles, gliosis and
CC neuronal loss. Hu-Asp1 protease substrate is useful for assaying
CC hu-Asp1 proteolytic activity, by contacting hu-Asp1 protein with
CC the substrate under acidic conditions and determining the level of
CC hu-Asp1 proteolytic activity. The present sequence is human aspartyl
CC protease-1 (hu-Asp-1) beta-secretase, wild-type peptide which is used
CC for determining the enzymatic activity of Asp-1 protein lacking a
CC transmembrane (TM) domain and containing (His)6 tag.
XX
SQ Sequence 8 AA;

Query Match 100.0%; Score 40; DB 22; Length 8;
Best Local Similarity 100.0%; Pred. No. 9.3e+05;
Matches 8; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

Qy 1 EVKMDAEF 8
||||||||
Db 1 EVKMDAEF 8

RESULT 3
AAE06902
ID AAE06902 standard; peptide; 8 AA.
XX
AC AAE06902;
XX
DT 23-OCT-2001 (first entry)
XX
DE Human amyloid precursor protein (APP) substrate peptide.
XX
KW Human; aspartyl protease 2; Asp 2; beta-amyloid precursor protein; APP;
KW beta-secretase; Alzheimer's disease; dementia; amyloid plaque; gliosis;
KW neurofibrillary tangle; neuronal loss; amyloid-beta peptide; nootropic;
KW neuroprotective; antisense therapy; gene therapy.
XX
OS Homo sapiens.
XX
PN WO200150829-A2.
XX
PD 19-JUL-2001.
XX
PF 09-MAY-2001; 2001WO-IB00799.
XX
PR 09-MAY-2001; 2001WO-IB00799.
XX
PA (BIEN/) BIENKOWSKI M J.
PA (GURN/) GURNEY M E.
PA (HEIN/) HEINRIKSON R L.
PA (PARO/) PARODI L A.

PA (YANR/) YAN R.
XX
PI Bienkowski MJ, Gurney ME, Heinrikson RL, Parodi LA, Yan R;
XX
DR WPI; 2001-483072/52.
XX
PT Novel purified polypeptide comprising fragment of mammalian aspartyl
PT protease 2, lacking Asp2 transmembrane domain and retaining beta
PT secretase activity of Asp2 useful for identifying inhibitors of Asp2
PT activity -
XX
PS Claim 128; Page 101; 185pp; English.
XX
CC The invention relates to human aspartyl proteases (Hu-Asp), beta-amyloid
CC precursor protein (APP) isoforms and their corresponding DNA molecules.
CC Human aspartyl proteases can act as beta-secretase proteases useful for
CC treating Alzheimer's disease. APP isoforms are useful for identifying
CC modulators of amyloid-beta peptide production, for use in designing
CC therapeutics for the treatment and prevention of Alzheimer's disease,
CC dementia, formation of amyloid plaques, neurofibrillary tangles, gliosis
CC and neuronal loss. APP isoforms are also used in methods for identifying
CC inhibitors and modulators of human Asp2 activity. The invention relates
CC to a method for identifying agents that modulate the activity of human
CC aspartyl protease Asp2. Amyloid-beta peptides obtained from APP are used
CC as a means to screen in cellular assays for the inhibitors of beta- and
CC gamma- secretase. Hu-Asp DNA fragments are useful as probes or primers in
CC polymerase chain reactions (PCR). The probes are useful for detecting
CC Hu-Asp nucleic acids in in vitro assays and in Northern and Southern
CC blots. The present sequence is human amyloid precursor protein (APP)
CC substrate peptide related to the invention.
XX
SQ Sequence 8 AA;

Query Match 100.0%; Score 40; DB 22; Length 8;
Best Local Similarity 100.0%; Pred. No. 9.3e+05;
Matches 8; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

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Qy          1 EVKMDAEF 8
              ||||||||
Db          1 EVKMDAEF 8
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RESULT 4
AAU06631
ID AAU06631 standard; Peptide; 8 AA.
XX
AC AAU06631;
XX
DT 24-OCT-2001 (first entry)
XX
DE Beta secretase substrate peptide.
XX
KW Aspartyl protease; Asp2; beta-secretase; nootropic;
KW neuroprotective; amyloid protein precursor; APP; Alzheimer's disease;
KW amyloid-beta; Abeta; Beta secretase substrate peptide.
XX
OS Synthetic.

XX
PN WO200149098-A2.
XX
PD 12-JUL-2001.
XX
PF 09-MAY-2001; 2001WO-IB00798.
XX
PR 09-MAY-2001; 2001WO-IB00798.
XX
PA (BIEN/) BIENKOWSKI M J.
PA (GURN/) GURNEY M E.
PA (HEIN/) HEINRIKSON R L.
PA (PARO/) PARODI L A.
PA (YANR/) YAN R.
XX
PI Bienkowski MJ, Gurney ME, Heinrikson RL, Parodi LA, Yan R;
XX
DR WPI; 2001-502549/55.
XX
PT Novel purified polypeptide comprising fragment of mammalian aspartyl
PT protease 2, lacking Asp2 transmembrane domain and retaining beta
PT secretase activity of Asp2 useful for identifying inhibitors of Asp2
PT activity -
XX
PS Claim 88; Page 94; 185pp; English.
XX
CC The invention relates to a purified polypeptide comprising a fragment of
CC mammalian aspartyl protease (Asp)2 protein which lacks the Asp2
CC transmembrane domain and the Asp2 protein, and where the polypeptide and
CC the fragment retain the beta-secretase activity of the mammalian Asp2
CC protein. The invention also details polynucleotides for the Asp
CC proteins and vectors expressing them, and a polypeptide (isoform of
CC amyloid protein precursor (APP)) comprising the amino acid sequence of an
CC APP or its fragment containing an APP cleavage site recognizable by a
CC mammalian beta-secretase, and further comprising two lysine residues at
CC the carboxyl terminus of the amino acid sequence of the mammalian APP or
CC APP fragment. Also included in the invention are methods of identifying
CC modulators or inhibitors of Asp2. Modulators and inhibitors of Asp2 are
CC useful for treating Alzheimer's disease. APP is useful in methods for
CC identifying inhibitors or modulators of human Asp2 activity and
CC amyloid-beta (Abeta) peptide production. APP is also useful in designing
CC therapeutics for the treatment or prevention of Alzheimer's disease.
CC APP comprising the APP-Sw-beta-secretase peptide sequence (NLDA), which
CC is associated with increased levels of Abeta processing is useful in
CC assays relating the Alzheimer's research. The expression vector is useful
CC for recombinantly expressing APP. Nucleic acids that hybridise to
CC Asp oligonucleotides are useful as probes or primers. The probes are
CC useful for detecting Hu-Asp nucleic acids in in vitro assays and in
CC Northern and Southern blots. The present sequence is a Beta secretase
CC substrate peptide.
XX
SQ Sequence 8 AA;

Query Match 100.0%; Score 40; DB 22; Length 8;
Best Local Similarity 100.0%; Pred. No. 9.3e+05;
Matches 8; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

```
Qy          1 EVKMDAEF 8
              ||||||||
Db          1 EVKMDAEF 8


RESULT 5
AAU06635
ID   AAU06635 standard; Peptide; 8 AA.
XX
AC   AAU06635;
XX
DT   24-OCT-2001  (first entry)
XX
DE   Synthetic fluorescent Asp2 substrate.
XX
KW   Aspartyl protease; Asp2; beta-secretase; nootropic;
KW   neuroprotective; amyloid protein precursor; APP; Alzheimer's disease;
KW   amyloid-beta; Abeta.
XX
OS   Synthetic.
XX
FH   Key             Location/Qualifiers
FT   Modified-site   1
FT                   /note= "Glu is covalently linked to a fluorescent
FT                   MCA moiety"
FT   Modified-site   8
FT                   /note= "Glu is covalently linked to a fluorescent
FT                   K-DNP moiety"
XX
PN   WO200149098-A2.
XX
PD   12-JUL-2001.
XX
PF   09-MAY-2001; 2001WO-IB00798.
XX
PR   09-MAY-2001; 2001WO-IB00798.
XX
PA   (BIEN/) BIENKOWSKI M J.
PA   (GURN/) GURNEY M E.
PA   (HEIN/) HEINRIKSON R L.
PA   (PARO/) PARODI L A.
PA   (YANR/) YAN R.
XX
PI   Bienkowski MJ,  Gurney ME,  Heinrikson RL,  Parodi LA,  Yan R;
XX
DR   WPI; 2001-502549/55.
XX
PT   Novel purified polypeptide comprising fragment of mammalian aspartyl
PT   protease 2, lacking Asp2 transmembrane domain and retaining beta
PT   secretase activity of Asp2 useful for identifying inhibitors of Asp2
PT   activity  -
XX
PS   Example 12; Page 81; 185pp; English.
XX
CC   The invention relates to a purified polypeptide comprising a fragment of
CC   mammalian aspartyl protease (Asp)2 protein which lacks the Asp2
CC   transmembrane domain and the Asp2 protein, and where the polypeptide and
```

CC the fragment retain the beta-secretase activity of the mammalian Asp2
CC protein. The invention also details polynucleotides for the Asp
CC proteins and vectors expressing them, and a polypeptide (isoform of
CC amyloid protein precursor (APP)) comprising the amino acid sequence of an
CC APP or its fragment containing an APP cleavage site recognizable by a
CC mammalian beta-secretase, and further comprising two lysine residues at
CC the carboxyl terminus of the amino acid sequence of the mammalian APP or
CC APP fragment. Also included in the invention are methods of identifying
CC modulators or inhibitors of Asp2. Modulators and inhibitors of Asp2 are
CC useful for treating Alzheimer's disease. APP is useful in methods for
CC identifying inhibitors or modulators of human Asp2 activity and
CC amyloid-beta (Abeta) peptide production. APP is also useful in designing
CC therapeutics for the treatment or prevention of Alzheimer's disease.
CC APP comprising the APP-Sw-beta-secretase peptide sequence (NLDA), which
CC is associated with increased levels of Abeta processing is useful in
CC assays relating the Alzheimer's research. The expression vector is useful
CC for recombinantly expressing APP. Nucleic acids that hybridise to
CC Asp oligonucleotides are useful as probes or primers. The probes are
CC useful for detecting Hu-Asp nucleic acids in in vitro assays and in
CC Northern and Southern blots. The present sequence is a synthetic
CC fluorescent substrate used to assay Asp2.
XX
SQ Sequence 8 AA;

Query Match 100.0%; Score 40; DB 22; Length 8;
Best Local Similarity 100.0%; Pred. No. 9.3e+05;
Matches 8; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

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Qy          1 EVKMDAEF 8
              ||||||||
Db          1 EVKMDAEF 8
```

RESULT 6
AAU07230
ID AAU07230 standard; Peptide; 8 AA.
XX
AC AAU07230;
XX
DT 24-OCT-2001 (first entry)
XX
DE Human beta-amyloid protein precursor, APP-beta secretase site peptide #3.
XX
KW Human; aspartyl protease 1; Asp-1; nootropic; neuroprotective;
KW aspartyl protease 2; Asp2; amyloid protein precursor; APP;
KW beta-secretase; Alzheimer's disease; APP-beta.
XX
OS Homo sapiens.
XX
PN WO200149097-A2.
XX
PD 12-JUL-2001.
XX
PF 09-MAY-2001; 2001WO-IB00797.
XX
PR 09-MAY-2001; 2001WO-IB00797.
XX

PA (BIEN/) BIENKOWSKI M J.
PA (GURN/) GURNEY M E.
PA (HEIN/) HEINRIKSON R L.
PA (PARO/) PARODI L A.
PA (YANR/) YAN R.
XX
PI Bienkowski MJ, Gurney ME, Heinrikson RL, Parodi LA, Yan R;
XX
DR WPI; 2001-502548/55.
XX
PT Novel purified polypeptide comprising fragment of mammalian aspartyl
PT protease 2, lacking Asp2 transmembrane domain and retaining beta
PT secretase activity of Asp2 useful for identifying inhibitors of Asp2
PT activity -
XX
PS Claim 88; Page 94; 185pp; English.
XX
CC The invention relates to a novel purified polypeptide comprising a
CC fragment of mammalian aspartyl protease 2 (Asp2) protein which lacks the
CC Asp2 transmembrane domain and the Asp2 protein, and where the polypeptide
CC and the fragment retain the beta-secretase activity of the mammalian Asp2
CC protein. Also included is an isoform of amyloid protein precursor (APP)
CC comprising the amino acid sequence of a APP or its fragment containing
CC an APP cleavage site recognisable by a mammalian beta-secretase, and
CC further comprising two lysine residues at the carboxyl terminus of the
CC amino acid sequence of the mammalian APP or APP fragment. The
CC polypeptides are used for assaying for modulators of beta-secretase
CC activity; identifying agents that inhibit the APP processing activity
CC of human Asp2 aspartyl protease (Hu-Asp2); identifying agents that
CC modulate the activity of Asp2; and for reducing cellular production of
CC amyloid beta (Abeta) from APP. Agents identified by the above methods
CC are useful for treating Alzheimer's disease; and for identifying
CC modulators of amyloid-beta (Abeta) peptide production, for use in
CC designing therapeutics for the treatment or prevention of Alzheimer's
CC disease. Probes and primers derived from Asp nucleic acid sequences
CC are useful for detecting Hu-Asp nucleic acids in in vitro assays and in
CC Northern and Southern blots. The present sequence represents the
CC amino acid sequence of human amyloid protein precursor, APP-beta
CC secretase site peptide substrate #3 used in assays of human Asp2 beta-
CC secretase activity.
XX
SQ Sequence 8 AA;

Query Match 100.0%; Score 40; DB 22; Length 8;
Best Local Similarity 100.0%; Pred. No. 9.3e+05;
Matches 8; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

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Qy          1 EVKMDAEF 8
              ||||||||
Db          1 EVKMDAEF 8
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RESULT 7
AAE02612
ID AAE02612 standard; peptide; 8 AA.
XX
AC AAE02612;

XX
DT 10-AUG-2001 (first entry)
XX
DE Human Aspartyl protease-1 (hu-Asp-1) beta-secretase, wild-type peptide.
XX
KW Human; alpha-secretase; amyloid precursor protein; APP; therapy;
KW Alzheimer's disease; antialzheimer's; aspartyl protease 1; Asp1;
KW beta-secretase.
XX
OS Homo sapiens.
XX
FH Key Location/Qualifiers
FT Cleavage-site 4..5
XX
PN WO200123533-A2.
XX
PD 05-APR-2001.
XX
PF 22-SEP-2000; 2000WO-US26080.
XX
PR 23-SEP-1999; 99US-0155493.
PR 23-SEP-1999; 99WO-US20881.
PR 13-OCT-1999; 99US-0416901.
PR 06-DEC-1999; 99US-0169232.
XX
PA (PHAA) PHARMACIA & UPJOHN CO.
XX
PI Gurney M, Bienkowski MJ;
XX
DR WPI; 2001-290516/30.
XX
PT Enzymes that cleave the alpha-secretase site of the amyloid precursor
PT protein, useful for the treatment of Alzheimer's disease -
XX
PS Example 15; Page 94; 189pp; English.
XX
CC The present invention relates to enzymes for cleaving the alpha-
CC secretase site of the amyloid precursor protein (APP) and methods of
CC identifying those enzymes. The methods may be used to identify enzymes
CC that may be used to cleave the alpha-secretase cleavage site of the APP
CC protein. The enzymes may be used to treat or modulate the progress of
CC Alzheimer's disease. The present sequence is human Aspartyl protease-1
CC (hu-Asp-1) beta-secretase, wild-type peptide which is used for
CC determining the enzymatic activity of Asp-1 deltaTM (His)6 protein.
XX
SQ Sequence 8 AA;

Query Match 100.0%; Score 40; DB 22; Length 8;
Best Local Similarity 100.0%; Pred. No. 9.3e+05;
Matches 8; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

```
Qy          1 EVKMDAEF 8
              ||||||||
Db          1 EVKMDAEF 8
```

RESULT 8

ABB78621
ID ABB78621 standard; Peptide; 8 AA.
XX
AC ABB78621;
XX
DT 16-JUL-2002 (first entry)
XX
DE APP Swedish mutant form beta-secretase processing site SEQ ID NO:70.
XX
KW Human; Asp-1; Asp-2; aspartyl protease; Alzheimer's disease;
KW proteolytic.
XX
OS Synthetic.
XX
PN GB2367060-A.
XX
PD 27-MAR-2002.
XX
PF 29-OCT-2001; 2001GB-0025934.
XX
PR 23-SEP-1999; 99US-155493P.
PR 23-SEP-1999; 99US-0404133.
PR 23-SEP-1999; 99WO-US20881.
PR 13-OCT-1999; 99US-0416901.
PR 06-DEC-1999; 99US-169232P.
PR 22-SEP-2000; 2000GB-0023315.
XX
PA (PHAA) PHARMACIA & UPJOHN CO.
XX
PI Bienkowkski MJ, Gurney M;
XX
DR WPI; 2002-396337/43.
XX
PT Human aspartyl protease 1 substrates useful in assays to detect
PT aspartyl protease activity, e.g. for the diagnosis of Alzheimer's
PT disease -
XX
PS Example 12; Page 85; 182pp; English.
XX
CC The present invention describes a human aspartyl protease 1 (hu-Asp1)
CC substrate (I) which comprises a peptide of no more than 50 amino acids,
CC and which comprises the 8 amino acid sequence Gly-Leu-Ala-Leu-Ala-Leu-
CC Glu-Pro. Also described are: (1) a method (II) for assaying hu-Asp1
CC proteolytic activity, comprising: (a) contacting a hu-Asp1 protein with
CC (I) under acidic conditions; and (b) determining the level of hu-Asp1
CC proteolytic activity; (2) a purified polynucleotide (III) comprising a
CC nucleotide sequence that hybridises under stringent conditions to the
CC non-coding strand complementary to a defined 1804 nucleotide sequence
CC (see ABL52456) where the nucleotide sequence encodes a polypeptide having
CC Asp1 proteolytic activity and lacks nucleotides encoding a transmembrane
CC domain); (3) a purified polynucleotide (III') comprising a sequence that
CC hybridises under stringent conditions to (III) (the nucleotide sequence
CC encodes a polypeptide further lacking a pro-peptide domain corresponding
CC to amino acids 23-62 of hu-Asp1 (see ABB78589)); (4) a vector (IV)
CC comprising (III) or (III'); and (5) a host cell (V) transformed or
CC transfected with (III), (III') and/or (IV). The hu-Asp1 protease
CC substrate (I) may be used as an enzyme substrate in assays to detect

CC aspartyl protease activity, (II) and therefore diagnose diseases
CC associated with aberrant hu-Asp1 expression and activity such as
CC Alzheimer's disease. Hu-Asp1 has been localised to chromosome 21, while
CC hu-Asp2 has been localised to chromosome 11q23.3-24.1. The present
CC sequence represents the amino acid sequence of a peptide that includes
CC the beta-secretase processing site within the Swedish mutant form of
CC amyloid precursor protein (APP), which is used in an example from the
CC present invention.
XX
SQ Sequence 8 AA;

Query Match 100.0%; Score 40; DB 23; Length 8;
Best Local Similarity 100.0%; Pred. No. 9.3e+05;
Matches 8; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

```
Qy          1 EVKMDAEF 8
              ||||||||
Db          1 EVKMDAEF 8
```

RESULT 9
AAW82083
ID AAW82083 standard; peptide; 9 AA.
XX
AC AAW82083;
XX
DT 18-FEB-1999 (first entry)
XX
DE Fluorogenic protease indicator protease binding peptide #61.
XX
KW Protease activity; fluorphore; detection; fluorogenic; cellular uptake;
KW conformation change.
XX
OS Synthetic.
XX
PN WO9837226-A1.
XX
PD 27-AUG-1998.
XX
PF 20-FEB-1998; 98WO-US03000.
XX
PR 20-FEB-1997; 97US-0802981.
XX
PA (ONCO-) ONCOIMMUNIN INC.
XX
PI Komoriya A, Packard BS;
XX
DR WPI; 1998-467579/40.
XX
PT New fluorogenic compositions - containing 2 fluorophores separated
PT by a peptide comprising a protease binding site, used for detecting
PT protease activity in samples.
XX
PS Claim 4; Page 77; 90pp; English.
XX
CC AAW82023-W82240 are peptides used in the construction of a fluorogenic
CC composition which is used for the detection of protease activity in

CC biological samples. The products can be used for the detection of
CC conformation changes in nucleic acids, oligosaccharides,
CC polysaccharides, proteins, peptides, lipids, phopholipids, glycolipids,
CC glycoproteins, steroids or polymers. In addition, attachment of a
CC hydrophobic group to a molecule can be used to enhance uptake by cells.
CC The composition is composed of P = peptide comprising a protease binding
CC site for the protease, F1, F2 peptides = fluorophores where F1 is
CC attached to the amino terminal amino acid and F2 is attached to the
CC carboxyl terminal amino acid and S1, S2 peptides = when present, are
CC peptide spacers where S1, when present, is attached to the amino terminal
CC acid, and S2, when present, is attached to the carboxyl terminal amino
CC acid.
XX
SQ Sequence 9 AA;

Query Match 100.0%; Score 40; DB 19; Length 9;
Best Local Similarity 100.0%; Pred. No. 9.3e+05;
Matches 8; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

Qy 1 EVKMDAEF 8
||||||||
Db 2 EVKMDAEF 9

RESULT 10
AAB07873
ID AAB07873 standard; peptide; 9 AA.
XX
AC AAB07873;
XX
DT 14-NOV-2000 (first entry)
XX
DE A peptide fragment derived from beta-amyloid precursor protein.
XX
KW Beta-secretase; beta-amyloid precursor protein; beta-amyloid peptide;
KW amyloid plaque component; Alzheimer's disease; amyloidogenic disease;
KW inhibitor.
XX
OS Homo sapiens.
XX
PN WO200047618-A2.
XX
PD 17-AUG-2000.
XX
PF 10-FEB-2000; 2000WO-US03819.
XX
PR 10-FEB-1999; 99US-0119571.
PR 15-JUN-1999; 99US-0139172.
XX
PA (ELAN-) ELAN PHARM INC.
XX
PI Anderson JP, Basi G, Doane MT, Frigon N, John V, Power M;
PI Sinha S, Tatsuno G, Tung J, Wang S, McConlogue L;
XX
DR WPI; 2000-533011/48.
XX
PT Purified beta-secretase protein used in assays to discover inhibitors

PT which can be used for the treatment of amyloidogenic diseases e.g.
PT Alzheimer's disease -
XX
PS Disclosure; Page 12; 121pp; English.
XX
CC The specification describes a beta-secretase enzyme. The enzyme cleaves
CC beta-amyloid precursor protein to produce beta-amyloid peptide. This
CC enzyme is therefore implicated in the production of amyloid plaque
CC components which accumulate in the brains of individuals afflicted with
CC Alzheimer's disease. Inhibitors of beta-secretase are administered to
CC a mammalian subject e.g. with Alzheimer's disease or Alzheimer's
CC disease-like pathology to test if they maintain or improve cognitive
CC ability or reduce the plaque burden. The compounds are used for the
CC treatment of amyloidogenic diseases e.g. Alzheimer's disease. The
CC present sequence represents a peptide derived from beta-amyloid
CC precursor protein
XX
SQ Sequence 9 AA;

Query Match 100.0%; Score 40; DB 21; Length 9;
Best Local Similarity 100.0%; Pred. No. 9.3e+05;
Matches 8; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

```
Qy          1 EVKMDAEF 8
              ||||||||
Db          2 EVKMDAEF 9
```

RESULT 11
AAY87949
ID AAY87949 standard; protein; 9 AA.
XX
AC AAY87949;
XX
DT 11-SEP-2000 (first entry)
XX
DE Mammalian amyloid precursor protein substrate peptide.
XX
KW Amyloid precursor protein; APP; secretase; vesicle; Abeta peptide;
KW Alzheimer's disease.
XX
OS Mammalia.
XX
PN WO200023576-A2.
XX
PD 27-APR-2000.
XX
PF 15-OCT-1999; 99WO-US24403.
XX
PR 16-OCT-1998; 98US-0173887.
PR 20-APR-1999; 99US-0294987.
XX
PA (HOOK/) HOOK V Y H.
XX
PI Hook VYH;
XX
DR WPI; 2000-339679/29.

XX
PT Determining the proteolytic activity of secretase for treating
PT Alzheimer's disease comprises permeablizing vesicles and incubating
PT with amyloid precursor protein (APP) to determine cleavage of APP
PT substrate -
XX
PS Example XV; Page 97; 97pp; English.
XX
CC This invention describes a novel method for the determination of
CC the proteolytic activity of a secretase comprising obtaining and
CC permeablizing pure vesicles, incubating the vesicles with an amyloid
CC precursor protein (APP) and determining the cleavage of the APP
CC substrate where the amount of cleavage is proportional to the
CC proteolytic activity of the secretase. The methods are useful for
CC selecting secretases and agents that cleave the amyloid precursor
CC protein substrate, inhibiting production of the Abeta peptide found
CC in Alzheimer's disease and treating Alzheimer's disease in patients.
CC This sequence represents a mammalian amyloid precursor protein, APP
CC substrate which is used in the method of the invention.
XX
SQ Sequence 9 AA;

Query Match 100.0%; Score 40; DB 21; Length 9;
Best Local Similarity 100.0%; Pred. No. 9.3e+05;
Matches 8; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

```
Qy          1 EVKMDAEF 8
              ||||||||
Db          2 EVKMDAEF 9
```

RESULT 12
ABU60430
ID ABU60430 standard; Peptide; 9 AA.
XX
AC ABU60430;
XX
DT 29-APR-2003 (first entry)
XX
DE Protease binding peptide motif SEQ ID 142.
XX
KW Protease; indicator; chromophore; H-dimer; fluorescence; absorbance;
KW nuclease; screening; fluorophore; substrate cleavage.
XX
OS Synthetic.
XX
PN WO200261038-A2.
XX
PD 08-AUG-2002.
XX
PF 21-DEC-2001; 2001WO-US49781.
XX
PR 22-DEC-2000; 2000US-0747287.
XX
PA (ONCO-) ONCOIMMUNIN INC.
XX
PI Packard BS, Komoriya A;

XX
DR WPI; 2002-698548/75.
XX
PT Indicator composition comprising polypeptide or nucleic acid backbone
PT joining two same chromophores resulting in quenching of fluorescence
PT of/change in absorbance of chromophores, useful for detecting protease
PT activity -
XX
PS Disclosure; Page 34; 97pp; English.
XX
CC This invention describes a novel indicator composition (referred as
CC homo-doubly labeled compositions) comprising a polypeptide backbone or
CC a nucleic acid backbone joining two chromophores of the same species
CC whereby the chromophores form an H-dimer resulting in quenching of the
CC fluorescence of or a change in the absorbance of the chromophore, a
CC decrease in fluorescence or a change in absorbance indicates that the
CC first molecule and the second molecule are interacting. The indicator is
CC useful for detecting the activity of a protease, where an increase in
CC fluorescence or a change in absorbance indicates that the protease
CC cleaves the polypeptide backbone. The indicator is attached to a solid
CC support inside a mammalian, yeast or insect cell. The composition bears a
CC hydrophobic group such as Fmoc, 9-fluoreneacetyl group,
CC 1-fluorenecarboxylic group, 9-florenecarboxylic group, and
CC 9-fluorenone-1-carboxylic group, benzyloxycarbonyl, Xanthyl (Xan), Trityl
CC (Trt), 4-methyltrityl (Mtt), 4-methoxytrityl (Mmt), 4-methoxy-2,3,
CC 6-trimethyl-benzenesulphonyl (Mtr), Mesitylene-2-sulphonyl (Mts),
CC 4,4'-dimethoxybenzhydryl (Mbh), etc. The method described in the
CC invention is useful for detecting protease or nuclease activity (or the
CC presence of nucleic acid) in histological section, cells in culture,
CC (e.g., seeded or cultured adherent cells), a biological sample such as
CC tissue, biopsy, lymph, embryo, or whole animal, or cell suspension
CC derived from a biological sample such as tissue, blood, urine, saliva,
CC lymph, or biopsy. The indicator composition is also useful for screening
CC a test agent for the ability to modulate a protease (or a nuclease,
CC lipase, etc.). The indicator reagents allow rapid determination of
CC protease activity in a matter of minutes in a single-step procedure. The
CC fluorescent indicators both absorb and emit in the visible range (400-800
CC nm). These signals are therefore not readily quenched by, nor is
CC activation of the fluorophores, that is, absorption of light, interfered
CC with by background molecules; therefore they are easily detected in
CC biological samples. The fluorogenic protease indicators utilise high
CC efficiency fluorophores and are able to achieve a high degree of
CC quenching while providing a strong signal when the quench is released by
CC cleavage of the peptide substrate. The high signal allows detection of
CC very low levels of protease activity. Thus the fluorogenic protease
CC indicators are particularly well suited for in situ detection of protease
CC activity. ABU60357-ABU60477 represent peptides use to illustrate the
CC method described in the disclosure of the invention.
XX
SQ Sequence 9 AA;

Query Match 100.0%; Score 40; DB 23; Length 9;
Best Local Similarity 100.0%; Pred. No. 9.3e+05;
Matches 8; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

Qy 1 EVKMDAEF 8
||||||||

Db 2 EVKMDAEF 9

RESULT 13
AAR22054
ID AAR22054 standard; peptide; 10 AA.
XX
AC AAR22054;
XX
DT 25-MAR-2003 (updated)
DT 06-JUL-1992 (first entry)
XX
DE Peptide P1.
XX
KW Beta amyloid; protein precursor; protease; Alzheimers disease;
KW radioiodination;
XX
OS Synthetic.
XX
FH Key Location/Qualifiers
FT Modified-site 1
FT /note= "site of radioiodination"
XX
PN WO9203542-A.
XX
PD 05-MAR-1992.
XX
PF 19-AUG-1991; 91WO-UO05932.
XX
PR 17-AUG-1990; 90US-0568806.
XX
PA (UYBO-) UNIV BOSTON.
XX
PI Abraham CR;
XX
DR WPI; 1992-096886/12.
XX
PT Treatment and diagnosis of Alzheimer's disease - by reducing
PT beta-protein precursor proteolysis near beta-protein N-terminus
PT by administering proteolysis inhibitor
XX
PS Disclosure; Page 6; 29pp; English.
XX
CC The synthetic peptide substrate P1 was used to assay for proteases
CC that cleave in the vicinity of the N-terminus of the amyloid beta
CC protein. The peptide corresponds to the beta protein precursor
CC sequence flanking that site. The peptide starts five amino acids
CC upstream from the N-terminus (at Asp) of the beta protein, and
CC extends across the putative cleavage site into the beta protein
CC itself. Histidine was substituted for the native isoleucine to give
CC a site for radioiodination. Labelled peptide was incubated with
CC brain fractions from Alzheimers disease patients. The resulting
CC fragments were separated by TLC and N-terminal fragments detected by
CC autoradiography.
CC See also AAR22055,6.
CC (Updated on 25-MAR-2003 to correct PA field.)
XX

```
SQ   Sequence   10 AA;

  Query Match             100.0%;  Score 40;  DB 13;  Length 10;
  Best Local Similarity   100.0%;  Pred. No. 0.024;
  Matches    8;  Conservative    0;  Mismatches    0;  Indels    0;  Gaps    0;

Qy          1 EVKMDAEF 8
              ||||||||
Db          3 EVKMDAEF 10


RESULT 14
AAR24261
ID   AAR24261 standard; Protein; 10 AA.
XX
AC   AAR24261;
XX
DT   25-MAR-2003  (updated)
DT   09-NOV-1992  (first entry)
XX
DE   Human amyloidin protease substrate sequence #1.
XX
KW   Alzheimer's disease; beta amyloid precursor protein; APP; zinc;
KW   metalloprotease; hAP; protease inhibitor; APP592-601
XX
OS   Synthetic.
XX
FH   Key             Location/Qualifiers
FT   Modified-site   1
FT                   /note= "Acetylated-Ser"
XX
PN   WO9207068-A1.
XX
PD   30-APR-1992.
XX
PF   04-OCT-1991;   91WO-US07290.
XX
PR   05-OCT-1990;   90US-0594122.
PR   30-SEP-1991;   91US-0766351.
XX
PA   (ATHE-) ATHENA NEUROSCIENCES INC.
PA   (ELIL ) LILLY & CO ELI.
XX
PI   Dovey HF,  Johnstone EM,  Little SP,  McConlogue L,  Seubert PA;
PI   Sinha S;
XX
DR   WPI; 1992-167148/20.
XX
PT   Human amyloidin protease - used for cleaving Met-Asp bond in
PT   amyloid-like substrate for identifying protease inhibitors
XX
PS   Claim 1; Page 52; 62pp; English.
XX
CC   Claimed human amyloidin protease is defined by its ability to
CC   cleave the Met-Asp bond of this synthetic substrate. The substrate,
CC   which corresponds to residues 592 to 601 of the 695 amino acid APP,
CC   can be used in an assay for identifying inhibitors of proteases
```

CC which cleave Met-Asp bonds, e.g. amyloidin, human skin chymase or
CC rat mast cell protease I or II.
CC See AAR24260-3, AAR24266-7 and AAQ24875-Q24887.
CC (Updated on 25-MAR-2003 to correct PN field.)
XX
SQ Sequence 10 AA;

Query Match 100.0%; Score 40; DB 13; Length 10;
Best Local Similarity 100.0%; Pred. No. 0.024;
Matches 8; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

Qy 1 EVKMDAEF 8
||||||||
Db 2 EVKMDAEF 9

RESULT 15
AAW82440
ID AAW82440 standard; peptide; 10 AA.
XX
AC AAW82440;
XX
DT 24-FEB-1999 (first entry)
XX
DE Human amyloid beta-protein N-terminal domain peptide P1.
XX
KW Amyloid beta-protein precursor; endoprotease; human; brain; screening;
KW Alzheimer's disease; O-phenanthroline; metal chelator; treatment;
KW pheymethylsulphonyl fluoride; protease inhibitor.
XX
OS Homo sapiens.
XX
PN US5849560-A.
XX
PD 15-DEC-1998.
XX
PF 26-FEB-1993; 93US-0025321.
XX
PR 26-FEB-1993; 93US-0025321.
PR 17-AUG-1990; 90US-0568806.
PR 05-APR-1991; 91US-0681093.
XX
PA (UYBO-) UNIV BOSTON.
XX
PI Abraham CR;
XX
DR WPI; 1999-069739/06.
XX
PT Purified endoprotease associated with Alzheimer's disease - is
PT prepared from fractions of brain tissue homogenate and is useful for
PT drug screening
XX
PS Claim 1; Column 17-18; 27pp; English.
XX
CC This sequence is the N-terminal domain of the amyloid beta-protein
CC precursor which is cleaved by a purified endoprotease from human brain
CC tissue homogenate and is identical to an endoprotease found in the

CC brains of humans with Alzheimer's disease. The endoprotease is inhibited
CC by O-phenanthroline and by metal chelators and is not inhibited by
CC pheymethylsulphonyl fluoride. The endoprotease is useful to screen for
CC protease inhibitors that might be useful for treating Alzheimer's disease
CC by inhibiting cleavage of the N-terminal domain of amyloid beta -protein
CC precursor.
XX
SQ Sequence 10 AA;

Query Match 100.0%; Score 40; DB 20; Length 10;
Best Local Similarity 100.0%; Pred. No. 0.024;
Matches 8; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

```
Qy          1 EVKMDAEF 8
              ||||||||
Db          3 EVKMDAEF 10
```

Search completed: January 21, 2004, 09:22:26
Job time : 2.1109 secs

GenCore version 5.1.6

OM protein - protein search, using sw model

Run on: January 21, 2004, 09:19:55 ; Search time 0.718929 Seconds
(without alignments)
470.821 Million cell updates/sec

Title: US-09-869-414A-67
Perfect score: 40
Sequence: 1 EVKMDAEF 8

Scoring table: BLOSUM62
Gapop 10.0 , Gapext 0.5

Searched: 328717 seqs, 42310858 residues

Total number of hits satisfying chosen parameters: 328717

Minimum DB seq length: 0
Maximum DB seq length: 2000000000

Post-processing: Minimum Match 0%
Maximum Match 100%
Listing first 45 summaries

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4: /cgn2_6/ptodata/1/iaa/6B_COMB.pep:*
5: /cgn2_6/ptodata/1/iaa/PCTUS_COMB.pep:*
6: /cgn2_6/ptodata/1/iaa/backfiles1.pep:*

Pred. No. is the number of results predicted by chance to have a score greater than or equal to the score of the result being printed, and is derived by analysis of the total score distribution.

SUMMARIES

Result No.	Score	% Query Match	Length	DB	ID	Description
1	40	100.0	8	4	US-09-548-372D-67	Sequence 67, Appl
2	40	100.0	8	4	US-09-548-367D-67	Sequence 67, Appl
3	40	100.0	8	4	US-09-551-853D-67	Sequence 67, Appl
4	40	100.0	9	3	US-08-802-981-221	Sequence 221, App
5	40	100.0	9	4	US-09-294-987-6	Sequence 6, Appli
6	40	100.0	10	2	US-08-025-321C-1	Sequence 1, Appli
7	40	100.0	10	4	US-09-548-372D-64	Sequence 64, Appl
8	40	100.0	10	4	US-09-548-367D-64	Sequence 64, Appl
9	40	100.0	10	4	US-09-551-853D-64	Sequence 64, Appl
10	40	100.0	10	4	US-09-604-608-4	Sequence 4, Appli
11	40	100.0	11	5	PCT-US94-07043A-7	Sequence 7, Appli

12	40	100.0	12	5	PCT-US94-07043A-2	Sequence 2, Appli
13	40	100.0	15	4	US-09-548-372D-71	Sequence 71, Appl
14	40	100.0	15	4	US-09-548-367D-71	Sequence 71, Appl
15	40	100.0	15	4	US-09-551-853D-71	Sequence 71, Appl
16	40	100.0	16	5	PCT-US94-07043A-1	Sequence 1, Appli
17	40	100.0	21	3	US-08-802-981-114	Sequence 114, App
18	40	100.0	27	1	US-08-141-324-11	Sequence 11, Appl
19	40	100.0	27	1	US-08-541-902-11	Sequence 11, Appl
20	40	100.0	45	1	US-08-462-859A-5	Sequence 5, Appli
21	40	100.0	45	1	US-08-123-659A-5	Sequence 5, Appli
22	40	100.0	45	1	US-08-464-247A-5	Sequence 5, Appli
23	40	100.0	45	1	US-08-464-248A-5	Sequence 5, Appli
24	40	100.0	58	1	US-08-371-930-25	Sequence 25, Appl
25	40	100.0	58	5	PCT-US94-01712-25	Sequence 25, Appl
26	40	100.0	59	1	US-08-484-969-3	Sequence 3, Appli
27	40	100.0	59	1	US-08-472-627-3	Sequence 3, Appli
28	40	100.0	59	1	US-08-388-463-3	Sequence 3, Appli
29	40	100.0	63	1	US-08-462-859A-3	Sequence 3, Appli
30	40	100.0	63	1	US-08-462-859A-4	Sequence 4, Appli
31	40	100.0	63	1	US-08-123-659A-3	Sequence 3, Appli
32	40	100.0	63	1	US-08-123-659A-4	Sequence 4, Appli
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34	40	100.0	63	1	US-08-464-247A-4	Sequence 4, Appli
35	40	100.0	63	1	US-08-464-248A-3	Sequence 3, Appli
36	40	100.0	63	1	US-08-464-248A-4	Sequence 4, Appli
37	40	100.0	103	2	US-08-404-831-2	Sequence 2, Appli
38	40	100.0	103	2	US-08-612-785B-2	Sequence 2, Appli
39	40	100.0	103	2	US-08-475-579A-2	Sequence 2, Appli
40	40	100.0	103	2	US-08-920-162A-2	Sequence 2, Appli
41	40	100.0	103	3	US-08-339-708A-10	Sequence 10, Appl
42	40	100.0	103	3	US-09-356-931-2	Sequence 2, Appli
43	40	100.0	103	4	US-08-703-675C-2	Sequence 2, Appli
44	40	100.0	103	4	US-08-617-267C-2	Sequence 2, Appli
45	40	100.0	105	2	US-08-729-345-1	Sequence 1, Appli

ALIGNMENTS

RESULT 1
US-09-548-372D-67
; Sequence 67, Application US/09548372D
; Patent No. 6420534
; GENERAL INFORMATION:
; APPLICANT: GURNEY ET AL.
; TITLE OF INVENTION: ALZHEIMER'S DISEASE SECRETASE, APP SUBSTRATES THEREFOR AND USES
; TITLE OF INVENTION: THEREOF
; FILE REFERENCE: 29915/6280I
; CURRENT APPLICATION NUMBER: US/09/548,372D
; CURRENT FILING DATE: 2000-04-12
; PRIOR APPLICATION NUMBER: US 60/155,493
; PRIOR FILING DATE: 1999-09-23
; PRIOR APPLICATION NUMBER: US 09/404,133
; PRIOR FILING DATE: 1999-09-23
; PRIOR APPLICATION NUMBER: PCT/US99/20881
; PRIOR FILING DATE: 1999-09-23

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;  PRIOR APPLICATION NUMBER: US 60/101,594
;  PRIOR FILING DATE: 1998-09-24
;  NUMBER OF SEQ ID NOS: 73
;  SOFTWARE: PatentIn version 3.1
; SEQ ID NO 67
;   LENGTH: 8
;   TYPE: PRT
;   ORGANISM: Artificial sequence
;   FEATURE:
;   OTHER INFORMATION: Peptide
US-09-548-372D-67

  Query Match             100.0%;  Score 40;  DB 4;  Length 8;
  Best Local Similarity   100.0%;  Pred. No. 2.5e+05;
  Matches    8;  Conservative    0;  Mismatches    0;  Indels    0;  Gaps    0;

Qy          1 EVKMDAEF 8
              ||||||||
Db          1 EVKMDAEF 8


RESULT 2
US-09-548-367D-67
; Sequence 67, Application US/09548367D
; Patent No. 6440698
; GENERAL INFORMATION:
;  APPLICANT: GURNEY ET AL.
;  TITLE OF INVENTION: ALZHEIMER'S DISEASE SECRETASE, APP SUBSTRATES THEREFOR
AND USES
;  TITLE OF INVENTION:  THEREOF
;  FILE REFERENCE: 29915/6280H
;  CURRENT APPLICATION NUMBER: US/09/548,367D
;  CURRENT FILING DATE:  2000-04-12
;  PRIOR APPLICATION NUMBER: US 60/155,493
;  PRIOR FILING DATE: 1999-09-23
;  PRIOR APPLICATION NUMBER: US 09/404,133
;  PRIOR FILING DATE: 1999-09-23
;  PRIOR APPLICATION NUMBER: PCT/US99/20881
;  PRIOR FILING DATE: 1999-09-23
;  PRIOR APPLICATION NUMBER: US 60/101,594
;  PRIOR FILING DATE: 1998-09-24
;  NUMBER OF SEQ ID NOS: 73
;  SOFTWARE: PatentIn version 3.1
; SEQ ID NO 67
;   LENGTH: 8
;   TYPE: PRT
;   ORGANISM: Artificial sequence
;   FEATURE:
;   OTHER INFORMATION: Peptide
US-09-548-367D-67

  Query Match             100.0%;  Score 40;  DB 4;  Length 8;
  Best Local Similarity   100.0%;  Pred. No. 2.5e+05;
  Matches    8;  Conservative    0;  Mismatches    0;  Indels    0;  Gaps    0;

Qy          1 EVKMDAEF 8
              ||||||||
```

```
Db          1 EVKMDAEF 8


RESULT 3
US-09-551-853D-67
; Sequence 67, Application US/09551853D
; Patent No. 6500667
; GENERAL INFORMATION:
;  APPLICANT: GURNEY ET AL.
;  TITLE OF INVENTION: ALZHEIMER'S DISEASE SECRETASE, APP SUBSTRATES THEREFOR
AND USES
;  TITLE OF INVENTION:  THEREOF
;  FILE REFERENCE: 29915/6280L
;  CURRENT APPLICATION NUMBER: US/09/551,853D
;  CURRENT FILING DATE:  2000-04-18
;  PRIOR APPLICATION NUMBER: US 60/155,493
;  PRIOR FILING DATE: 1999-09-23
;  PRIOR APPLICATION NUMBER: US 09/404,133
;  PRIOR FILING DATE: 1999-09-23
;  PRIOR APPLICATION NUMBER: PCT/US99/20881
;  PRIOR FILING DATE: 1999-09-23
;  PRIOR APPLICATION NUMBER: US 60/101,594
;  PRIOR FILING DATE: 1998-09-24
;  NUMBER OF SEQ ID NOS: 73
;  SOFTWARE: PatentIn version 3.1
; SEQ ID NO 67
;   LENGTH: 8
;   TYPE: PRT
;   ORGANISM: Artificial sequence
;   FEATURE:
;   OTHER INFORMATION: Peptide
US-09-551-853D-67

  Query Match             100.0%;  Score 40;  DB 4;  Length 8;
  Best Local Similarity   100.0%;  Pred. No. 2.5e+05;
  Matches    8;  Conservative    0;  Mismatches    0;  Indels    0;  Gaps    0;

Qy          1 EVKMDAEF 8
              ||||||||
Db          1 EVKMDAEF 8


RESULT 4
US-08-802-981-221
; Sequence 221, Application US/08802981
; Patent No. 6037137
;  GENERAL INFORMATION:
;    APPLICANT:  Komoriya, Akira
;    APPLICANT:  Packard, Beverly S.
;    TITLE OF INVENTION:  Compositions for the Detection of Enzyme
;    TITLE OF INVENTION:  Activity in Biological Samples and Methods of Use
Thereof
;    NUMBER OF SEQUENCES:  231
;    CORRESPONDENCE ADDRESS:
;      ADDRESSEE:  Townsend and Townsend and Crew LLP
;      STREET:  Two Embarcadero Center, Eighth Floor
;      CITY:  San Francisco
```

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;       STATE:  California
;       COUNTRY:  USA
;       ZIP:  94111-3834
;     COMPUTER READABLE FORM:
;       MEDIUM TYPE:  Floppy disk
;       COMPUTER:  IBM PC compatible
;       OPERATING SYSTEM:  PC-DOS/MS-DOS
;       SOFTWARE:  PatentIn Release #1.0, Version #1.30
;     CURRENT APPLICATION DATA:
;       APPLICATION NUMBER:  US/08/802,981
;       FILING DATE:  20-FEB-1997
;       CLASSIFICATION:  435
;     ATTORNEY/AGENT INFORMATION:
;       NAME:  Hunter, Tom
;       REGISTRATION NUMBER:  38,498
;       REFERENCE/DOCKET NUMBER:  016865-000300US
;     TELECOMMUNICATION INFORMATION:
;       TELEPHONE:  (415) 576-0200
;       TELEFAX:  (415) 576-0300
;   INFORMATION FOR SEQ ID NO:  221:
;     SEQUENCE CHARACTERISTICS:
;       LENGTH:  9 amino acids
;       TYPE:  amino acid
;       STRANDEDNESS:
;       TOPOLOGY:  linear
;     MOLECULE TYPE:  peptide
US-08-802-981-221

  Query Match             100.0%;  Score 40;  DB 3;  Length 9;
  Best Local Similarity   100.0%;  Pred. No. 2.5e+05;
  Matches    8;  Conservative    0;  Mismatches    0;  Indels    0;  Gaps    0;

Qy          1 EVKMDAEF 8
              ||||||||
Db          2 EVKMDAEF 9


RESULT 5
US-09-294-987-6
; Sequence 6, Application US/09294987
; Patent No. 6313268
; GENERAL INFORMATION:
;  APPLICANT:  Hook, Vivian Y.H.
;  TITLE OF INVENTION:  SECRETASES RELATED TO ALZHEIMER'S DEMENTIA
;  FILE REFERENCE:  P-AS 3515
;  CURRENT APPLICATION NUMBER: US/09/294,987
;  CURRENT FILING DATE:  1999-04-20
;  PRIOR APPLICATION NUMBER:  US 09/173,887
;  PRIOR FILING DATE:  1998-10-16
;  NUMBER OF SEQ ID NOS:  6
;  SOFTWARE:  PatentIn Ver. 2.0
; SEQ ID NO 6
;   LENGTH: 9
;   TYPE: PRT
;   ORGANISM: mammalian
US-09-294-987-6
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  Query Match             100.0%;  Score 40;  DB 4;  Length 9;
  Best Local Similarity   100.0%;  Pred. No. 2.5e+05;
  Matches    8;  Conservative    0;  Mismatches    0;  Indels    0;  Gaps    0;

Qy          1 EVKMDAEF 8
              ||||||||
Db          2 EVKMDAEF 9


RESULT 6
US-08-025-321C-1
; Sequence 1, Application US/08025321C
; Patent No. 5849560
;  GENERAL INFORMATION:
;    APPLICANT:  Abraham Ph.D., Carmela R.
;    TITLE OF INVENTION:  PROTEASES CAUSING ABNORMAL DEGREDATION
;    TITLE OF INVENTION:  OF AMYLOID BETA-PROTEIN PRECURSOR
;    NUMBER OF SEQUENCES:  13
;    CORRESPONDENCE ADDRESS:
;      ADDRESSEE:  Choate, Hall & Stewart
;      STREET:  53 State Street
;      CITY:  Boston
;      STATE:  MA
;      COUNTRY:  USA
;      ZIP:  02109
;    COMPUTER READABLE FORM:
;      MEDIUM TYPE:  Floppy disk
;      COMPUTER:  IBM PC compatible
;      OPERATING SYSTEM:  PC-DOS/MS-DOS
;      SOFTWARE:  PatentIn Release #1.0, Version #1.30
;    CURRENT APPLICATION DATA:
;      APPLICATION NUMBER:  US/08/025,321C
;      FILING DATE:  26-FEB-1993
;      CLASSIFICATION:  435
;    ATTORNEY/AGENT INFORMATION:
;      NAME:  Jarrell Ph.D., Brenda H.
;      REGISTRATION NUMBER:  39,223
;      REFERENCE/DOCKET NUMBER:  0079571-0034
;    TELECOMMUNICATION INFORMATION:
;      TELEPHONE:  617 248 5000
;      TELEFAX:  617 248 4000
;  INFORMATION FOR SEQ ID NO:  1:
;    SEQUENCE CHARACTERISTICS:
;      LENGTH:  10 amino acids
;      TYPE:  amino acid
;      STRANDEDNESS:  not relevant
;      TOPOLOGY:  not relevant
;    MOLECULE TYPE:  peptide
US-08-025-321C-1

  Query Match             100.0%;  Score 40;  DB 2;  Length 10;
  Best Local Similarity   100.0%;  Pred. No. 0.015;
  Matches    8;  Conservative    0;  Mismatches    0;  Indels    0;  Gaps    0;

Qy          1 EVKMDAEF 8
              ||||||||
Db          3 EVKMDAEF 10
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RESULT 7
US-09-548-372D-64
; Sequence 64, Application US/09548372D
; Patent No. 6420534
; GENERAL INFORMATION:
; APPLICANT: GURNEY ET AL.
; TITLE OF INVENTION: ALZHEIMER'S DISEASE SECRETASE, APP SUBSTRATES THEREFOR
AND USES
; TITLE OF INVENTION: THEREOF
; FILE REFERENCE: 29915/6280I
; CURRENT APPLICATION NUMBER: US/09/548,372D
; CURRENT FILING DATE: 2000-04-12
; PRIOR APPLICATION NUMBER: US 60/155,493
; PRIOR FILING DATE: 1999-09-23
; PRIOR APPLICATION NUMBER: US 09/404,133
; PRIOR FILING DATE: 1999-09-23
; PRIOR APPLICATION NUMBER: PCT/US99/20881
; PRIOR FILING DATE: 1999-09-23
; PRIOR APPLICATION NUMBER: US 60/101,594
; PRIOR FILING DATE: 1998-09-24
; NUMBER OF SEQ ID NOS: 73
; SOFTWARE: PatentIn version 3.1
; SEQ ID NO 64
;   LENGTH: 10
;   TYPE: PRT
;   ORGANISM: Artificial sequence
;   FEATURE:
;   OTHER INFORMATION: Synthetic peptide
US-09-548-372D-64

  Query Match   100.0%; Score 40; DB 4; Length 10;
  Best Local Similarity   100.0%; Pred. No. 0.015;
  Matches   8; Conservative   0; Mismatches   0; Indels   0; Gaps   0;

Qy   1 EVKMDAEF 8
              ||||||||
Db   2 EVKMDAEF 9

RESULT 8
US-09-548-367D-64
; Sequence 64, Application US/09548367D
; Patent No. 6440698
; GENERAL INFORMATION:
; APPLICANT: GURNEY ET AL.
; TITLE OF INVENTION: ALZHEIMER'S DISEASE SECRETASE, APP SUBSTRATES THEREFOR
AND USES
; TITLE OF INVENTION: THEREOF
; FILE REFERENCE: 29915/6280H
; CURRENT APPLICATION NUMBER: US/09/548,367D
; CURRENT FILING DATE: 2000-04-12
; PRIOR APPLICATION NUMBER: US 60/155,493
; PRIOR FILING DATE: 1999-09-23
; PRIOR APPLICATION NUMBER: US 09/404,133
; PRIOR FILING DATE: 1999-09-23

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;  PRIOR APPLICATION NUMBER: PCT/US99/20881
;  PRIOR FILING DATE: 1999-09-23
;  PRIOR APPLICATION NUMBER: US 60/101,594
;  PRIOR FILING DATE: 1998-09-24
;  NUMBER OF SEQ ID NOS: 73
;  SOFTWARE: PatentIn version 3.1
; SEQ ID NO 64
;   LENGTH: 10
;   TYPE: PRT
;   ORGANISM: Artificial sequence
;   FEATURE:
;   OTHER INFORMATION: Synthetic peptide
US-09-548-367D-64

  Query Match             100.0%;  Score 40;  DB 4;  Length 10;
  Best Local Similarity   100.0%;  Pred. No. 0.015;
  Matches    8;  Conservative    0;  Mismatches    0;  Indels    0;  Gaps    0;

Qy          1 EVKMDAEF 8
              ||||||||
Db          2 EVKMDAEF 9


RESULT 9
US-09-551-853D-64
; Sequence 64, Application US/09551853D
; Patent No. 6500667
; GENERAL INFORMATION:
;  APPLICANT: GURNEY ET AL.
;  TITLE OF INVENTION: ALZHEIMER'S DISEASE SECRETASE, APP SUBSTRATES THEREFOR
AND USES
;  TITLE OF INVENTION:  THEREOF
;  FILE REFERENCE: 29915/6280L
;  CURRENT APPLICATION NUMBER: US/09/551,853D
;  CURRENT FILING DATE:  2000-04-18
;  PRIOR APPLICATION NUMBER: US 60/155,493
;  PRIOR FILING DATE: 1999-09-23
;  PRIOR APPLICATION NUMBER: US 09/404,133
;  PRIOR FILING DATE: 1999-09-23
;  PRIOR APPLICATION NUMBER: PCT/US99/20881
;  PRIOR FILING DATE: 1999-09-23
;  PRIOR APPLICATION NUMBER: US 60/101,594
;  PRIOR FILING DATE: 1998-09-24
;  NUMBER OF SEQ ID NOS: 73
;  SOFTWARE: PatentIn version 3.1
; SEQ ID NO 64
;   LENGTH: 10
;   TYPE: PRT
;   ORGANISM: Artificial sequence
;   FEATURE:
;   OTHER INFORMATION: Synthetic peptide
US-09-551-853D-64

  Query Match             100.0%;  Score 40;  DB 4;  Length 10;
  Best Local Similarity   100.0%;  Pred. No. 0.015;
  Matches    8;  Conservative    0;  Mismatches    0;  Indels    0;  Gaps    0;
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Qy          1 EVKMDAEF 8
              ||||||||
Db          2 EVKMDAEF 9


RESULT 10
US-09-604-608-4
; Sequence 4, Application US/09604608
; Patent No. 6545127
; GENERAL INFORMATION:
;  APPLICANT:  Tang, Jordan J.N.
;  APPLICANT:  Lin, Xinli
;  APPLICANT:  Koelsch, Gerald
;  TITLE OF INVENTION:  Catalytically Active Recombinant Memapsin and Methods
;  TITLE OF INVENTION:  of Use Thereof
;  FILE REFERENCE:  OMRF 179
;  CURRENT APPLICATION NUMBER: US/09/604,608
;  CURRENT FILING DATE:  2000-06-27
;  PRIOR APPLICATION NUMBER:  60/141,363
;  PRIOR FILING DATE:  1999-06-28
;  PRIOR APPLICATION NUMBER:  60/168,060
;  PRIOR FILING DATE:  1999-11-30
;  PRIOR APPLICATION NUMBER:  60/177,836
;  PRIOR FILING DATE:  2000-01-25
;  PRIOR APPLICATION NUMBER:  60/178,368
;  PRIOR FILING DATE:  2000-01-27
;  PRIOR APPLICATION NUMBER:  60/210,292
;  PRIOR FILING DATE:  2000-06-08
;  NUMBER OF SEQ ID NOS:  31
;  SOFTWARE:  PatentIn Ver. 2.1
; SEQ ID NO 4
;   LENGTH: 10
;   TYPE: PRT
;   ORGANISM: Artificial Sequence
;   FEATURE:
;   OTHER INFORMATION: Description of Artificial Sequence: Primer
US-09-604-608-4

  Query Match             100.0%;  Score 40;  DB 4;  Length 10;
  Best Local Similarity   100.0%;  Pred. No. 0.015;
  Matches    8;  Conservative    0;  Mismatches    0;  Indels    0;  Gaps    0;

Qy          1 EVKMDAEF 8
              ||||||||
Db          2 EVKMDAEF 9


RESULT 11
PCT-US94-07043A-7
; Sequence 7, Application PC/TUS9407043A
;  GENERAL INFORMATION:
;    APPLICANT:  Tamburini, Paul P.; Benz, G nter; H bich,
;    APPLICANT:  Dieter; Dreyer, Robert N.; Koenig, Gerhard
;    TITLE OF INVENTION:  CATHEPSIN D IS AN AMYLOIDOGENIC
;    TITLE OF INVENTION:  PROTEASE IN ALZHEIMER S DISEASE
;    NUMBER OF SEQUENCES:  11
;    CORRESPONDENCE ADDRESS:
```

```
;       ADDRESSEE:  Miles Inc.
;       STREET:  400 Morgan Lane
;       CITY:  West Haven
;       STATE:  Connecticut
;       COUNTRY:  USA
;       ZIP:  06516
;     COMPUTER READABLE FORM:
;       MEDIUM TYPE:  Diskette, 3.50 inch, 800 kb storage
;       COMPUTER:  Sharp PC 4600
;       OPERATING SYSTEM:  MS-DOS
;       SOFTWARE:  WordPerfect 5.1
;     CURRENT APPLICATION DATA:
;       APPLICATION NUMBER:  PCT/US94/07043A
;       FILING DATE:  June 21, 1994
;       CLASSIFICATION:
;     PRIOR APPLICATION DATA:
;       APPLICATION NUMBER:  PCT/US93/10889
;       FILING DATE:  November 12, 1993
;     PRIOR APPLICATION DATA:
;       APPLICATION NUMBER:  07/995,660
;       FILING DATE:  December 16, 1992
;     PRIOR APPLICATION DATA:
;       APPLICATION NUMBER:  07/880,914
;       FILING DATE:  May 11, 1992
;     ATTORNEY/AGENT INFORMATION:
;       NAME:  Pamela A. Simonton
;       REGISTRATION NUMBER:  31,060
;       REFERENCE/DOCKET NUMBER:  MTI 224.3
;     TELECOMMUNICATION INFORMATION:
;       TELEPHONE:  (203) 937-2340
;       TELEFAX:  (203) 937-2795
;   INFORMATION FOR SEQ ID NO:  7:
;     SEQUENCE CHARACTERISTICS:
;       LENGTH:  11 amino acids
;       TYPE:  amino acid
;       TOPOLOGY:  linear
PCT-US94-07043A-7

  Query Match             100.0%;  Score 40;  DB 5;  Length 11;
  Best Local Similarity   100.0%;  Pred. No. 0.016;
  Matches    8;  Conservative    0;  Mismatches    0;  Indels    0;  Gaps    0;

Qy          1 EVKMDAEF 8
              ||||||||
Db          3 EVKMDAEF 10


RESULT 12
PCT-US94-07043A-2
; Sequence 2, Application PC/TUS9407043A
;  GENERAL INFORMATION:
;     APPLICANT:  Tamburini, Paul P.; Benz, G nter; H bich,
;     APPLICANT:  Dieter; Dreyer, Robert N.; Koenig, Gerhard
;     TITLE OF INVENTION:  CATHEPSIN D IS AN AMYLOIDOGENIC
;     TITLE OF INVENTION:  PROTEASE IN ALZHEIMER S DISEASE
;     NUMBER OF SEQUENCES:  11
;     CORRESPONDENCE ADDRESS:
```

; ADDRESSEE: Miles Inc.
; STREET: 400 Morgan Lane
; CITY: West Haven
; STATE: Connecticut
; COUNTRY: USA
; ZIP: 06516
; COMPUTER READABLE FORM:
; MEDIUM TYPE: Diskette, 3.50 inch, 800 kb storage
; COMPUTER: Sharp PC 4600
; OPERATING SYSTEM: MS-DOS
; SOFTWARE: WordPerfect 5.1
; CURRENT APPLICATION DATA:
; APPLICATION NUMBER: PCT/US94/07043A
; FILING DATE: June 21, 1994
; CLASSIFICATION:
; PRIOR APPLICATION DATA:
; APPLICATION NUMBER: PCT/US93/10889
; FILING DATE: November 12, 1993
; PRIOR APPLICATION DATA:
; APPLICATION NUMBER: 07/995,660
; FILING DATE: December 16, 1992
; PRIOR APPLICATION DATA:
; APPLICATION NUMBER: 07/880,914
; FILING DATE: May 11, 1992
; ATTORNEY/AGENT INFORMATION:
; NAME: Pamela A. Simonton
; REGISTRATION NUMBER: 31,060
; REFERENCE/DOCKET NUMBER: MTI 224.3
; TELECOMMUNICATION INFORMATION:
; TELEPHONE: (203) 937-2340
; TELEFAX: (203) 937-2795
; INFORMATION FOR SEQ ID NO: 2:
; SEQUENCE CHARACTERISTICS:
; LENGTH: 12 amino acids
; TYPE: amino acid
; TOPOLOGY: linear
PCT-US94-07043A-2

Query Match 100.0%; Score 40; DB 5; Length 12;
Best Local Similarity 100.0%; Pred. No. 0.018;
Matches 8; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

Qy 1 EVKMDAEF 8
||||||||
Db 3 EVKMDAEF 10

RESULT 13
US-09-548-372D-71
; Sequence 71, Application US/09548372D
; Patent No. 6420534
; GENERAL INFORMATION:
; APPLICANT: GURNEY ET AL.
; TITLE OF INVENTION: ALZHEIMER'S DISEASE SECRETASE, APP SUBSTRATES THEREFOR
AND USES
; TITLE OF INVENTION: THEREOF
; FILE REFERENCE: 29915/6280I

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;  CURRENT APPLICATION NUMBER: US/09/548,372D
;  CURRENT FILING DATE:  2000-04-12
;  PRIOR APPLICATION NUMBER: US 60/155,493
;  PRIOR FILING DATE: 1999-09-23
;  PRIOR APPLICATION NUMBER: US 09/404,133
;  PRIOR FILING DATE: 1999-09-23
;  PRIOR APPLICATION NUMBER: PCT/US99/20881
;  PRIOR FILING DATE: 1999-09-23
;  PRIOR APPLICATION NUMBER: US 60/101,594
;  PRIOR FILING DATE: 1998-09-24
;  NUMBER OF SEQ ID NOS: 73
;  SOFTWARE: PatentIn version 3.1
; SEQ ID NO 71
;   LENGTH: 15
;   TYPE: PRT
;   ORGANISM: Artificial sequence
;   FEATURE:
;   OTHER INFORMATION: peptide
US-09-548-372D-71

  Query Match             100.0%;  Score 40;  DB 4;  Length 15;
  Best Local Similarity   100.0%;  Pred. No. 0.022;
  Matches    8;  Conservative    0;  Mismatches    0;  Indels    0;  Gaps    0;

Qy          1 EVKMDAEF 8
              ||||||||
Db          4 EVKMDAEF 11


RESULT 14
US-09-548-367D-71
; Sequence 71, Application US/09548367D
; Patent No. 6440698
; GENERAL INFORMATION:
;  APPLICANT: GURNEY ET AL.
;  TITLE OF INVENTION: ALZHEIMER'S DISEASE SECRETASE, APP SUBSTRATES THEREFOR
AND USES
;  TITLE OF INVENTION:  THEREOF
;  FILE REFERENCE: 29915/6280H
;  CURRENT APPLICATION NUMBER: US/09/548,367D
;  CURRENT FILING DATE:  2000-04-12
;  PRIOR APPLICATION NUMBER: US 60/155,493
;  PRIOR FILING DATE: 1999-09-23
;  PRIOR APPLICATION NUMBER: US 09/404,133
;  PRIOR FILING DATE: 1999-09-23
;  PRIOR APPLICATION NUMBER: PCT/US99/20881
;  PRIOR FILING DATE: 1999-09-23
;  PRIOR APPLICATION NUMBER: US 60/101,594
;  PRIOR FILING DATE: 1998-09-24
;  NUMBER OF SEQ ID NOS: 73
;  SOFTWARE: PatentIn version 3.1
; SEQ ID NO 71
;   LENGTH: 15
;   TYPE: PRT
;   ORGANISM: Artificial sequence
;   FEATURE:
;   OTHER INFORMATION: peptide
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US-09-548-367D-71

  Query Match   100.0%; Score 40; DB 4; Length 15;
  Best Local Similarity   100.0%; Pred. No. 0.022;
  Matches   8; Conservative   0; Mismatches   0; Indels   0; Gaps   0;

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Qy          1 EVKMDAEF 8
              ||||||||
Db          4 EVKMDAEF 11
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RESULT 15
US-09-551-853D-71
; Sequence 71, Application US/09551853D
; Patent No. 6500667
; GENERAL INFORMATION:
; APPLICANT: GURNEY ET AL.
; TITLE OF INVENTION: ALZHEIMER'S DISEASE SECRETASE, APP SUBSTRATES THEREFOR AND USES
; TITLE OF INVENTION: THEREOF
; FILE REFERENCE: 29915/6280L
; CURRENT APPLICATION NUMBER: US/09/551,853D
; CURRENT FILING DATE: 2000-04-18
; PRIOR APPLICATION NUMBER: US 60/155,493
; PRIOR FILING DATE: 1999-09-23
; PRIOR APPLICATION NUMBER: US 09/404,133
; PRIOR FILING DATE: 1999-09-23
; PRIOR APPLICATION NUMBER: PCT/US99/20881
; PRIOR FILING DATE: 1999-09-23
; PRIOR APPLICATION NUMBER: US 60/101,594
; PRIOR FILING DATE: 1998-09-24
; NUMBER OF SEQ ID NOS: 73
; SOFTWARE: PatentIn version 3.1
; SEQ ID NO 71
;   LENGTH: 15
;   TYPE: PRT
;   ORGANISM: Artificial sequence
;   FEATURE:
;   OTHER INFORMATION: peptide
US-09-551-853D-71

  Query Match   100.0%; Score 40; DB 4; Length 15;
  Best Local Similarity   100.0%; Pred. No. 0.022;
  Matches   8; Conservative   0; Mismatches   0; Indels   0; Gaps   0;

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Qy          1 EVKMDAEF 8
              ||||||||
Db          4 EVKMDAEF 11
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Search completed: January 21, 2004, 09:27:08
Job time : 0.718929 secs

GenCore version 5.1.6

OM protein - protein search, using sw model

Run on: January 21, 2004, 09:16:55 ; Search time 0.734226 Seconds
(without alignments)
1047.838 Million cell updates/sec

Title: US-09-869-414A-67
Perfect score: 40
Sequence: 1 EVKMDAEF 8

Scoring table: BLOSUM62
Gapop 10.0 , Gapext 0.5

Searched: 283308 seqs, 96168682 residues

Total number of hits satisfying chosen parameters: 283308

Minimum DB seq length: 0
Maximum DB seq length: 2000000000

Post-processing: Minimum Match 0%
Maximum Match 100%
Listing first 45 summaries

Database : PIR_76:*
1: pir1:*
2: pir2:*
3: pir3:*
4: pir4:*

Pred. No. is the number of results predicted by chance to have a score greater than or equal to the score of the result being printed, and is derived by analysis of the total score distribution.

SUMMARIES

Result No.	Score	% Query Match	Length	DB	ID	Description
1	40	100.0	33	2	S23094	beta-amyloid prote
2	40	100.0	57	2	E60045	Alzheimer's diseas
3	40	100.0	57	2	F60045	Alzheimer's diseas
4	40	100.0	57	2	G60045	Alzheimer's diseas
5	40	100.0	57	2	D60045	Alzheimer's diseas
6	40	100.0	57	2	A60045	Alzheimer's diseas
7	40	100.0	57	2	B60045	Alzheimer's diseas
8	40	100.0	82	2	PQ0438	Alzheimer's diseas
9	40	100.0	695	1	A49795	Alzheimer's diseas
10	40	100.0	695	2	A27485	Alzheimer's diseas
11	40	100.0	695	2	S00550	Alzheimer's diseas
12	40	100.0	770	1	QRHUA4	Alzheimer's diseas
13	34	85.0	142	2	E89026	protein F13A2.1 [i

14	34	85.0	747	2	JH0773	Alzheimer's diseas
15	33	82.5	626	2	AF0358	conserved hypothet
16	32	80.0	354	2	S51143	FMO-protein - Chlo
17	32	80.0	426	2	G75187	probable trehalose
18	32	80.0	929	2	T52517	hypothetical prote
19	32	80.0	1906	2	AD2443	hypothetical prote
20	31	77.5	282	2	T26112	hypothetical prote
21	31	77.5	3562	2	A47171	chondroitin sulfat
22	30	75.0	233	2	T03329	probable amidase l
23	30	75.0	375	2	A83352	probable glyceroph
24	30	75.0	584	2	A97171	uncharacterized pr
25	30	75.0	627	2	AB0535	hypothetical prote
26	30	75.0	774	2	AG1565	autolysin (amidase
27	30	75.0	793	2	T27133	hypothetical prote
28	29	72.5	84	2	T27174	hypothetical prote
29	29	72.5	182	2	B97000	hypothetical prote
30	29	72.5	242	2	C96606	hypothetical prote
31	29	72.5	280	2	T09939	hypothetical prote
32	29	72.5	286	2	G85230	hypothetical prote
33	29	72.5	385	2	G97350	xylR transcription
34	29	72.5	400	2	E69446	hypothetical prote
35	29	72.5	408	2	F70369	carboxyl-terminal
36	29	72.5	452	2	S56938	fructose-2,6-bisph
37	29	72.5	463	2	T38111	atrazine chlorohyd
38	29	72.5	464	2	T38356	septin homolog spn
39	29	72.5	470	2	C75591	threonine synthase
40	29	72.5	491	2	F64118	cytosolic axial fi
41	29	72.5	526	2	D71805	protein-export mem
42	29	72.5	844	2	T32608	hypothetical prote
43	29	72.5	871	2	T43427	pob1 protein - fis
44	29	72.5	949	1	S55478	pyruvate, phosphat
45	29	72.5	1378	2	G88637	protein F53H1.4 [i

ALIGNMENTS

RESULT 1
S23094
beta-amyloid protein precursor - rat
C;Species: Rattus norvegicus (Norway rat)
C;Date: 22-Nov-1993 #sequence_revision 10-Nov-1995 #text_change 03-May-1996
C;Accession: S23094
R;Kojima, S.; Omori, M.
FEBS Lett. 304, 57-60, 1992
A;Title: Two-way cleavage of beta-amyloid protein precursor by multicatalytic proteinase.
A;Reference number: S23094; MUID:92316198; PMID:1618299
A;Accession: S23094
A;Molecule type: protein
A;Residues: 1-33 <KOJ>
C;Superfamily: Alzheimer's disease amyloid beta protein; animal Kunitz-type proteinase inhibitor homology

Query Match 100.0%; Score 40; DB 2; Length 33;
Best Local Similarity 100.0%; Pred. No. 0.024;
Matches 8; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

```
Qy          1 EVKMDAEF 8
              ||||||||
Db          2 EVKMDAEF 9
```

RESULT 2
E60045
Alzheimer's disease amyloid beta/A4 protein precursor - sheep (fragment)
C;Species: Ovis sp. (sheep)
C;Date: 01-Dec-1992 #sequence_revision 01-Dec-1992 #text_change 28-Jul-1995
C;Accession: E60045
R;Johnstone, E.M.; Chaney, M.O.; Norris, F.H.; Pascual, R.; Little, S.P.
Brain Res. Mol. Brain Res. 10, 299-305, 1991
A;Title: Conservation of the sequence of the Alzheimer's disease amyloid peptide in dog, polar bear and five other mammals by cross-species polymerase chain reaction analysis.
A;Reference number: A60045; MUID:92017079; PMID:1656157
A;Accession: E60045
A;Molecule type: mRNA
A;Residues: 1-57 <JOH>
A;Cross-references: EMBL:X56130
C;Superfamily: Alzheimer's disease amyloid beta protein; animal Kunitz-type proteinase inhibitor homology
C;Keywords: alternative splicing; Alzheimer's disease; amyloid; brain

```
  Query Match             100.0%;  Score 40;  DB 2;  Length 57;
  Best Local Similarity   100.0%;  Pred. No. 0.044;
  Matches    8;  Conservative    0;  Mismatches    0;  Indels    0;  Gaps    0;

Qy          1 EVKMDAEF 8
              ||||||||
Db          2 EVKMDAEF 9
```

RESULT 3
F60045
Alzheimer's disease amyloid beta/A4 protein precursor - pig (fragment)
C;Species: Sus scrofa domestica (domestic pig)
C;Date: 01-Dec-1992 #sequence_revision 01-Dec-1992 #text_change 13-Aug-1999
C;Accession: F60045
R;Johnstone, E.M.; Chaney, M.O.; Norris, F.H.; Pascual, R.; Little, S.P.
Brain Res. Mol. Brain Res. 10, 299-305, 1991
A;Title: Conservation of the sequence of the Alzheimer's disease amyloid peptide in dog, polar bear and five other mammals by cross-species polymerase chain reaction analysis.
A;Reference number: A60045; MUID:92017079; PMID:1656157
A;Accession: F60045
A;Molecule type: mRNA
A;Residues: 1-57 <JOH>
A;Cross-references: EMBL:X56127; NID:g1895; PIDN:CAA39592.1; PID:g1896
C;Superfamily: Alzheimer's disease amyloid beta protein; animal Kunitz-type proteinase inhibitor homology
C;Keywords: alternative splicing; Alzheimer's disease; amyloid; brain

```
  Query Match             100.0%;  Score 40;  DB 2;  Length 57;
  Best Local Similarity   100.0%;  Pred. No. 0.044;
```

Matches 8; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

```
Qy          1 EVKMDAEF 8
              ||||||||
Db          2 EVKMDAEF 9
```

RESULT 4
G60045
Alzheimer's disease amyloid beta/A4 protein precursor - guinea pig (fragment)
C;Species: Cavia porcellus (guinea pig)
C;Date: 01-Dec-1992 #sequence_revision 01-Dec-1992 #text_change 28-Jul-1995
C;Accession: G60045
R;Johnstone, E.M.; Chaney, M.O.; Norris, F.H.; Pascual, R.; Little, S.P.
Brain Res. Mol. Brain Res. 10, 299-305, 1991
A;Title: Conservation of the sequence of the Alzheimer's disease amyloid peptide in dog, polar bear and five other mammals by cross-species polymerase chain reaction analysis.
A;Reference number: A60045; MUID:92017079; PMID:1656157
A;Accession: G60045
A;Molecule type: mRNA
A;Residues: 1-57 <JOH>
A;Cross-references: EMBL:X56126
C;Superfamily: Alzheimer's disease amyloid beta protein; animal Kunitz-type proteinase inhibitor homology
C;Keywords: alternative splicing; Alzheimer's disease; amyloid; brain

Query Match 100.0%; Score 40; DB 2; Length 57;
Best Local Similarity 100.0%; Pred. No. 0.044;
Matches 8; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

```
Qy          1 EVKMDAEF 8
              ||||||||
Db          2 EVKMDAEF 9
```

RESULT 5
D60045
Alzheimer's disease amyloid beta/A4 protein precursor - bovine (fragment)
C;Species: Bos primigenius taurus (cattle)
C;Date: 01-Dec-1992 #sequence_revision 01-Dec-1992 #text_change 28-Jul-1995
C;Accession: D60045
R;Johnstone, E.M.; Chaney, M.O.; Norris, F.H.; Pascual, R.; Little, S.P.
Brain Res. Mol. Brain Res. 10, 299-305, 1991
A;Title: Conservation of the sequence of the Alzheimer's disease amyloid peptide in dog, polar bear and five other mammals by cross-species polymerase chain reaction analysis.
A;Reference number: A60045; MUID:92017079; PMID:1656157
A;Accession: D60045
A;Molecule type: mRNA
A;Residues: 1-57 <JOH>
A;Cross-references: EMBL:X56124
C;Superfamily: Alzheimer's disease amyloid beta protein; animal Kunitz-type proteinase inhibitor homology
C;Keywords: alternative splicing; Alzheimer's disease; amyloid; brain

Query Match 100.0%; Score 40; DB 2; Length 57;

Best Local Similarity 100.0%; Pred. No. 0.044;
Matches 8; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

```
Qy          1 EVKMDAEF 8
              ||||||||
Db          2 EVKMDAEF 9
```

RESULT 6
A60045
Alzheimer's disease amyloid beta/A4 protein precursor - dog (fragment)
C;Species: Canis lupus familiaris (dog)
C;Date: 01-Dec-1992 #sequence_revision 01-Dec-1992 #text_change 28-Jul-1995
C;Accession: A60045
R;Johnstone, E.M.; Chaney, M.O.; Norris, F.H.; Pascual, R.; Little, S.P.
Brain Res. Mol. Brain Res. 10, 299-305, 1991
A;Title: Conservation of the sequence of the Alzheimer's disease amyloid peptide in dog, polar bear and five other mammals by cross-species polymerase chain reaction analysis.
A;Reference number: A60045; MUID:92017079; PMID:1656157
A;Accession: A60045
A;Molecule type: mRNA
A;Residues: 1-57 <JOH>
A;Cross-references: EMBL:X56125
C;Superfamily: Alzheimer's disease amyloid beta protein; animal Kunitz-type proteinase inhibitor homology
C;Keywords: alternative splicing; Alzheimer's disease; amyloid; brain

Query Match 100.0%; Score 40; DB 2; Length 57;
Best Local Similarity 100.0%; Pred. No. 0.044;
Matches 8; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

```
Qy          1 EVKMDAEF 8
              ||||||||
Db          2 EVKMDAEF 9
```

RESULT 7
B60045
Alzheimer's disease amyloid beta/A4 protein precursor - polar bear (fragment)
C;Species: Ursus maritimus (polar bear)
C;Date: 01-Dec-1992 #sequence_revision 01-Dec-1992 #text_change 13-Aug-1999
C;Accession: B60045
R;Johnstone, E.M.; Chaney, M.O.; Norris, F.H.; Pascual, R.; Little, S.P.
Brain Res. Mol. Brain Res. 10, 299-305, 1991
A;Title: Conservation of the sequence of the Alzheimer's disease amyloid peptide in dog, polar bear and five other mammals by cross-species polymerase chain reaction analysis.
A;Reference number: A60045; MUID:92017079; PMID:1656157
A;Accession: B60045
A;Molecule type: mRNA
A;Residues: 1-57 <JOH>
A;Cross-references: EMBL:X56128; NID:g2165; PIDN:CAA39593.1; PID:g2166
C;Superfamily: Alzheimer's disease amyloid beta protein; animal Kunitz-type proteinase inhibitor homology
C;Keywords: alternative splicing; Alzheimer's disease; amyloid; brain

```
  Query Match             100.0%;  Score 40;  DB 2;  Length 57;
  Best Local Similarity   100.0%;  Pred. No. 0.044;
  Matches    8;  Conservative    0;  Mismatches    0;  Indels    0;  Gaps    0;

Qy          1 EVKMDAEF 8
              ||||||||
Db          2 EVKMDAEF 9
```

```
RESULT 8
PQ0438
Alzheimer's disease amyloid A4 protein precursor - rabbit (fragment)
C;Species: Oryctolagus cuniculus (domestic rabbit)
C;Date: 30-Sep-1993 #sequence_revision 19-Oct-1995 #text_change 19-Oct-1995
C;Accession: PQ0438; C60045
R;Davidson, J.S.; West, R.L.; Kotikalapudi, P.; Maroun, L.E.
Biochem. Biophys. Res. Commun. 188, 905-911, 1992
A;Title: Sequence and methylation in the beta/A4 region of the rabbit amyloid
precursor protein gene.
A;Reference number: PQ0438; MUID:93075180; PMID:1445331
A;Accession: PQ0438
A;Molecule type: DNA
A;Residues: 1-82 <DAV>
A;Cross-references: GB:M83558; GB:M83657
R;Johnstone, E.M.; Chaney, M.O.; Norris, F.H.; Pascual, R.; Little, S.P.
Brain Res. Mol. Brain Res. 10, 299-305, 1991
A;Title: Conservation of the sequence of the Alzheimer's disease amyloid peptide
in dog, polar bear and five other mammals by cross-species polymerase chain
reaction analysis.
A;Reference number: A60045; MUID:92017079; PMID:1656157
A;Accession: C60045
A;Molecule type: mRNA
A;Residues: 12-68 <JOH>
A;Cross-references: EMBL:X56129
C;Superfamily: Alzheimer's disease amyloid beta protein; animal Kunitz-type
proteinase inhibitor homology
C;Keywords: alternative splicing; Alzheimer's disease; amyloid; Down's syndrome
```

```
  Query Match             100.0%;  Score 40;  DB 2;  Length 82;
  Best Local Similarity   100.0%;  Pred. No. 0.066;
  Matches    8;  Conservative    0;  Mismatches    0;  Indels    0;  Gaps    0;

Qy          1 EVKMDAEF 8
              ||||||||
Db         13 EVKMDAEF 20
```

```
RESULT 9
A49795
Alzheimer's disease amyloid beta protein precursor - crab-eating macaque
C;Species: Macaca fascicularis (crab-eating macaque)
C;Date: 10-Sep-1999 #sequence_revision 10-Sep-1999 #text_change 10-Sep-1999
C;Accession: A49795
R;Podlisny, M.B.; Tolan, D.R.; Selkoe, D.J.
Am. J. Pathol. 138, 1423-1435, 1991
A;Title: Homology of the amyloid beta protein precursor in monkey and human
supports a primate model for beta amyloidosis in Alzheimer's disease.
```

A;Reference number: A49795; MUID:91273117; PMID:1905108
A;Accession: A49795
A;Status: preliminary
A;Molecule type: mRNA
A;Residues: 1-695 <POD>
A;Cross-references: GB:M58727; NID:g342062; PIDN:AAA36829.1; PID:g342063
C;Superfamily: Alzheimer's disease amyloid beta protein; animal Kunitz-type proteinase inhibitor homology
C;Keywords: alternative splicing

  Query Match 100.0%; Score 40; DB 1; Length 695;
  Best Local Similarity 100.0%; Pred. No. 0.69;
  Matches 8; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

Qy 1 EVKMDAEF 8
      ||||||||
Db 593 EVKMDAEF 600

RESULT 10
A27485
Alzheimer's disease amyloid beta/A4 protein homolog precursor - mouse
N;Alternate names: proteinase nexin II
C;Species: Mus musculus (house mouse)
C;Date: 31-Mar-1989 #sequence_revision 31-Mar-1989 #text_change 13-Aug-1999
C;Accession: A27485; S19727; I49485
R;Yamada, T.; Sasaki, H.; Furuya, H.; Miyata, T.; Goto, I.; Sakaki, Y.
Biochem. Biophys. Res. Commun. 149, 665-671, 1987
A;Title: Complementary DNA for the mouse homolog of the human amyloid beta protein precursor.
A;Reference number: A27485; MUID:88106489; PMID:3322280
A;Accession: A27485
A;Molecule type: mRNA
A;Residues: 1-695 <YAM>
A;Cross-references: GB:M18373; NID:g191568; PIDN:AAA37139.1; PID:g309085
A;Experimental source: brain
R;de Strooper, B.; van Leuven, F.; van den Berghe, H.
Biochim. Biophys. Acta 1129, 141-143, 1991
A;Title: The amyloid beta protein precursor or proteinase nexin II from mouse is closer related to its human homolog than previously reported.
A;Reference number: S19727; MUID:92096458; PMID:1756177
A;Accession: S19727
A;Molecule type: mRNA
A;Residues: 1-210,'G',212-220,'S',222-396,'A',398-402,'T',404-448,'A',450-695 <STR>
A;Cross-references: EMBL:X59379
R;Izumi, R.; Yamada, T.; Yoshikai, S.; Sasaki, H.; Hattori, M.; Sakaki, Y.
Gene 112, 189-195, 1992
A;Title: Positive and negative regulatory elements for the expression of the Alzheimer's disease amyloid precursor-encoding gene in mouse.
A;Reference number: I49485; MUID:92209998; PMID:1555768
A;Accession: I49485
A;Status: translated from GB/EMBL/DDBJ
A;Molecule type: DNA
A;Residues: 1-19 <RES>
A;Cross-references: GB:D10603; NID:g220328; PIDN:BAA01456.1; PID:g220329
C;Genetics:

A;Map position: 16C3
C;Superfamily: Alzheimer's disease amyloid beta protein; animal Kunitz-type proteinase inhibitor homology
C;Keywords: alternative splicing; amyloid; transmembrane protein

  Query Match 100.0%; Score 40; DB 2; Length 695;
  Best Local Similarity 100.0%; Pred. No. 0.69;
  Matches 8; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

Qy 1 EVKMDAEF 8
      ||||||||
Db 593 EVKMDAEF 600

RESULT 11
S00550
Alzheimer's disease amyloid beta protein precursor - rat
N;Alternate names: beta-A4 amyloid protein
C;Species: Rattus norvegicus (Norway rat)
C;Date: 30-Jun-1989 #sequence_revision 30-Jun-1989 #text_change 13-Aug-1999
C;Accession: S00550; A41245; A39820; S46251
R;Shivers, B.D.; Hilbich, C.; Multhaup, G.; Salbaum, M.; Beyreuther, K.; Seeburg, P.H.
EMBO J. 7, 1365-1370, 1988
A;Title: Alzheimer's disease amyloidogenic glycoprotein: expression pattern in rat brain suggests a role in cell contact.
A;Reference number: S00550; MUID:88312583; PMID:2900758
A;Accession: S00550
A;Molecule type: mRNA
A;Residues: 1-695 <SHI>
A;Cross-references: EMBL:X07648; NID:g55616; PIDN:CAA30488.1; PID:g55617
R;Schubert, D.; Schroeder, R.; LaCorbiere, M.; Saitoh, T.; Cole, G.
Science 241, 223-226, 1988
A;Title: Amyloid beta protein precursor is possibly a heparan sulfate proteoglycan core protein.
A;Reference number: A41245; MUID:88264430; PMID:2968652
A;Accession: A41245
A;Molecule type: protein
A;Residues: 18-37,'X',39-40,'X',42-44 <SCH>
A;Note: evidence for heparan sulfate attachment
R;Hesse, L.; Beher, D.; Masters, C.L.; Multhaup, G.
FEBS Lett. 349, 109-116, 1994
A;Title: The beta-A4 amyloid precursor protein binding to copper.
A;Reference number: S46251; MUID:94320627; PMID:7913895
A;Contents: annotation; copper binding sites
A;Note: rat peptides were isolated but not sequenced
R;Potempska, A.; Styles, J.; Mehta, P.; Kim, K.S.; Miller, D.L.
J. Biol. Chem. 266, 8464-8469, 1991
A;Title: Purification and tissue level of the beta-amyloid peptide precursor of rat brain.
A;Reference number: A39820; MUID:91217087; PMID:1673681
A;Accession: A39820
A;Status: preliminary
A;Molecule type: protein
A;Residues: 18-32 <POT>
A;Experimental source: brain

C;Comment: Deposition of amyloid protein as neurofibrillary tangles and/or plaques is characteristic of both Alzheimer's disease and Down's syndrome.
C;Superfamily: Alzheimer's disease amyloid beta protein; animal Kunitz-type proteinase inhibitor homology
C;Keywords: alternative splicing; amyloid; glycoprotein; transmembrane protein
F;625-648/Domain: transmembrane #status predicted <TMM>

Query Match 100.0%; Score 40; DB 2; Length 695;
Best Local Similarity 100.0%; Pred. No. 0.69;
Matches 8; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

```
Qy          1 EVKMDAEF 8
              ||||||||
Db        593 EVKMDAEF 600
```

RESULT 12
QRHUA4
Alzheimer's disease amyloid beta protein precursor [validated] - human
N;Alternate names: Alzheimer's disease amyloid A4 protein; coagulation factor XIa inhibitor; proteinase nexin II (PN-II)
N;Contains: amyloid beta protein long, plaque form; amyloid beta protein short, vascular form; amyloid protein precursor splice form APP(695); amyloid protein precursor splice form APP(751); amyloid protein precursor splice form APP(770)
C;Species: Homo sapiens (man)
C;Date: 30-Jun-1987 #sequence_revision 28-Jul-1995 #text_change 15-Sep-2000
C;Accession: S02260; S05194; A32277; A33260; A35486; I39452; I39451; I39453; I59562; A44017; B44017; A03134; A29030; A47584; A47585; S02638; S00707; S00925; A38949; A30320; B30320; C30320; A31087; A24668; A28583; A29302; A60805; JL0038; S06121; A60355; A59011; A38384; S29076; S38252; S32539; S48148; S48692; S51186; S51185; S51184; S51183; A54238; I58075; I52250; S09010; S10737; S24127; S43644
R;Lemaire, H.G.; Salbaum, J.M.; Multhaup, G.; Kang, J.; Bayney, R.M.; Unterbeck, A.; Beyreuther, K.; Mueller-Hill, B.
Nucleic Acids Res. 17, 517-522, 1989
A;Title: The PreA4(695) precursor protein of Alzheimer's disease A4 amyloid is encoded by 16 exons.
A;Reference number: S02260; MUID:89128427; PMID:2783775
A;Accession: S02260
A;Molecule type: DNA
A;Residues: 1-288,'V',365-770 <LEM1>
A;Cross-references: EMBL:X13466
A;Note: alternative splice form APP(695)
R;Lemaire, H.G.
submitted to the EMBL Data Library, November 1988
A;Reference number: S05194
A;Accession: S05194
A;Molecule type: DNA
A;Residues: 1-14,'VW',17-288,'V',365-770 <LEM2>
A;Cross-references: EMBL:X13466; NID:g35598; PIDN:CAA31830.1; PID:g871360
A;Note: alternative splice form APP(695)
R;La Fauci, G.; Lahiri, D.K.; Salton, S.R.J.; Robakis, N.K.
Biochem. Biophys. Res. Commun. 159, 297-304, 1989
A;Title: Characterization of the 5'-end region and the first two exons of the beta-protein precursor gene.
A;Reference number: A32277; MUID:89165870; PMID:2538123
A;Accession: A32277
A;Molecule type: DNA

A;Residues: 1-75 <LAF>
A;Cross-references: GB:M24546; GB:M24547; NID:g341202; PIDN:AAC13654.1;
PID:g516074
R;Johnstone, E.M.; Chaney, M.O.; Moore, R.E.; Ward, K.E.; Norris, F.H.; Little,
S.P.
Biochem. Biophys. Res. Commun. 163, 1248-1255, 1989
A;Title: Alzheimer's disease amyloid peptide is encoded by two exons and shows
similarity to soybean trypsin inhibitor.
A;Reference number: A33260; MUID:89392030; PMID:2675837
A;Accession: A33260
A;Molecule type: DNA
A;Residues: 656-737 <JOH>
A;Cross-references: GB:M29270; NID:g178863; PIDN:AAA51768.1; PID:g178865
R;Prelli, F.; Levy, E.; van Duinen, S.G.; Bots, G.T.A.M.; Luyendijk, W.;
Frangione, B.
Biochem. Biophys. Res. Commun. 170, 301-307, 1990
A;Title: Expression of a normal and variant Alzheimer's beta-protein gene in
amyloid of hereditary cerebral hemorrhage, Dutch type: DNA and protein
diagnostic assays.
A;Reference number: A35486; MUID:90321244; PMID:2196878
A;Accession: A35486
A;Molecule type: DNA
A;Residues: 672-710 <PRE1>
A;Note: 693-Gln was found in DNA isolated from HCHWA-D patients
R;Yoshikai, S.I.; Sasaki, H.; Doh-ura, K.; Furuya, H.; Sakaki, Y.
Gene 87, 257-263, 1990
A;Title: Genomic organization of the human amyloid beta-protein precursor gene.
A;Reference number: I39451; MUID:90236318; PMID:2110105
A;Accession: I39452
A;Status: nucleic acid sequence not shown; translation not shown; translated
from GB/EMBL/DDBJ
A;Molecule type: DNA
A;Residues: 1-770 <YOS1>
A;Cross-references: GB:M33112; NID:g178613; PIDN:AAB59502.1; PID:g178616
A;Accession: I39451
A;Status: nucleic acid sequence not shown; translation not shown; translated
from GB/EMBL/DDBJ
A;Molecule type: DNA
A;Residues: 1-530,'QWLMPVIPAFWEAKVGR' <YOS2>
A;Cross-references: GB:M34875; NID:g178608; PIDN:AAB59501.1; PID:g178615
R;Yoshikai, S.I.; Sasaki, H.; Doh-ura, K.; Furuya, H.; Sakaki, Y.
Gene 102, 291-292, 1991
A;Reference number: A59020; MUID:91340168; PMID:1908403
A;Contents: annotation; erratum
A;Note: revised physical map for reference I39451
R;Levy, E.; Carman, M.D.; Fernandez-Madrid, I.J.; Power, M.D.; Lieberburg, I.;
van Duinen, S.G.; Bots, G.T.; Luyendijk, W.; Frangione, B.
Science 248, 1124-1126, 1990
A;Title: Mutation of the Alzheimer's disease amyloid gene in hereditary cerebral
hemorrhage, Dutch type.
A;Reference number: I39453; MUID:90260663; PMID:2111584
A;Accession: I39453
A;Status: translated from GB/EMBL/DDBJ
A;Molecule type: DNA
A;Residues: 656-737 <LEV>
A;Cross-references: GB:M37896; NID:g178618; PIDN:AAA51727.1; PID:g178620
A;Note: a mutation with 693-Gln is presented

R;Murrell, J.; Farlow, M.; Ghetti, B.; Benson, M.D.
Science 254, 97-99, 1991
A;Title: A mutation in the amyloid precursor protein associated with hereditary Alzheimer's disease.
A;Reference number: I59562; MUID:92022553; PMID:1925564
A;Accession: I59562
A;Status: translated from GB/EMBL/DDBJ
A;Molecule type: DNA
A;Residues: 689-716,'F',718-737 <MUR>
A;Cross-references: GB:S57665; NID:g236720; PIDN:AAB19991.1; PID:g236721
R;Kamino, K.; Orr, H.T.; Payami, H.; Wijsman, E.M.; Alonso, M.E.; Pulst, S.M.; Anderson, L.; O'dahl, S.; Nemens, E.; White, J.A.; Sadovnick, A.D.; Ball, M.J.; Kaye, J.; Warren, A.; McInnis, M.; Antonarakis, S.E.; Korenberg, J.R.; Sharma, V.; Kukull, W.; Larson, E.; Heston, L.L.; Martin, G.M.; Bird, T.D.; Schellenberg, G.D.
Am. J. Hum. Genet. 51, 998-1014, 1992
A;Title: Linkage and mutational analysis of familial Alzheimer disease kindreds for the APP gene region.
A;Reference number: A44017; MUID:93035397; PMID:1415269
A;Accession: A44017
A;Molecule type: DNA
A;Residues: 687-692,'G',694-718 <KAM1>
A;Cross-references: GB:S45135; NID:g257377; PIDN:AAB23645.1; PID:g257378
A;Experimental source: familial Alzheimer disease family SB
A;Note: sequence extracted from NCBI backbone (NCBIP:115374)
A;Accession: B44017
A;Molecule type: DNA
A;Residues: 687-718 <KAM2>
A;Cross-references: GB:S45136; NID:g257379; PIDN:AAB23646.1; PID:g257380
A;Experimental source: familial Alzheimer disease family LIT
A;Note: sequence extracted from NCBI backbone (NCBIP:115376)
A;Note: this sequence has a silent mutation
R;Kang, J.; Lemaire, H.G.; Unterbeck, A.; Salbaum, J.M.; Masters, C.L.; Grzeschik, K.H.; Multhaup, G.; Beyreuther, K.; Muller-Hill, B.
Nature 325, 733-736, 1987
A;Title: The precursor of Alzheimer's disease amyloid A4 protein resembles a cell-surface receptor.
A;Reference number: A03134; MUID:87144572; PMID:2881207
A;Accession: A03134
A;Molecule type: mRNA
A;Residues: 1-288,'V',365-770 <KAN>
A;Cross-references: GB:Y00264; NID:g28525; PIDN:CAA68374.1; PID:g28526
A;Note: alternative splice form APP(695)
R;Robakis, N.K.; Ramakrishna, N.; Wolfe, G.; Wisniewski, H.M.
Proc. Natl. Acad. Sci. U.S.A. 84, 4190-4194, 1987
A;Title: Molecular cloning and characterization of a cDNA encoding the cerebrovascular and the neuritic plaque amyloid peptides.
A;Reference number: A29030; MUID:87231971; PMID:3035574
A;Accession: A29030
A;Molecule type: mRNA
A;Residues: 284-288,'V',365-646,'E',648-770 <ROB>
A;Cross-references: GB:M16765; NID:g178539; PIDN:AAA51722.1; PID:g178540
A;Note: the authors translated the codon GAG for residue 647 as Asp
R;Goldgaber, D.; Lerman, M.I.; McBride, O.W.; Saffiotti, U.; Gajdusek, D.C.
Science 235, 877-880, 1987
A;Title: Characterization and chromosomal localization of a cDNA encoding brain amyloid of Alzheimer's disease.

A;Reference number: A47584; MUID:87120328; PMID:3810169
A;Accession: A47584
A;Molecule type: mRNA
A;Residues: 674-756,'S',758-770 <GOL>
A;Cross-references: GB:M15533; NID:g178706; PIDN:AAA35540.1; PID:g178707
A;Experimental source: brain
R;Tanzi, R.E.; Gusella, J.F.; Watkins, P.C.; Bruns, G.A.P.; St George-Hyslop, P.; Van Keuren, M.L.; Patterson, D.; Pagan, S.; Kurnit, D.M.; Neve, R.L.
Science 235, 880-884, 1987
A;Title: Amyloid beta protein gene: cDNA, mRNA distribution, and genetic linkage near the Alzheimer locus.
A;Reference number: A47585; MUID:87120329; PMID:2949367
A;Accession: A47585
A;Molecule type: mRNA
A;Residues: 674-703 <TAN1>
A;Cross-references: GB:M15532; NID:g177957; PIDN:AAA51564.1; PID:g177958
R;Dyrks, T.; Weidemann, A.; Multhaup, G.; Salbaum, J.M.; Lemaire, H.G.; Kang, J.; Mueller-Hill, B.; Masters, C.L.; Beyreuther, K.
EMBO J. 7, 949-957, 1988
A;Title: Identification, transmembrane orientation and biogenesis of the amyloid A4 precursor of Alzheimer's disease.
A;Reference number: S02638; MUID:88296437; PMID:2900137
A;Accession: S02638
A;Molecule type: mRNA
A;Residues: 672-678 <DYR>
R;Tanzi, R.E.; McClatchey, A.I.; Lamperti, E.D.; Villa-Komaroff, L.; Gusella, J.F.; Neve, R.L.
Nature 331, 528-530, 1988
A;Title: Protease inhibitor domain encoded by an amyloid protein precursor mRNA associated with Alzheimer's disease.
A;Reference number: S00707; MUID:88122640; PMID:2893290
A;Accession: S00707
A;Molecule type: mRNA
A;Residues: 286-344,'I',365-366 <TAN2>
A;Cross-references: EMBL:X06982; NID:g28817; PIDN:CAA30042.1; PID:g929612
A;Experimental source: promyelocytic leukemia cell line HL60
A;Note: alternative splice form APP(751)
R;Ponte, P.; Gonzalez-DeWhitt, P.; Schilling, J.; Miller, J.; Hsu, D.; Greenberg, B.; Davis, K.; Wallace, W.; Lieberburg, I.; Fuller, F.; Cordell, B.
Nature 331, 525-527, 1988
A;Title: A new A4 amyloid mRNA contains a domain homologous to serine proteinase inhibitors.
A;Reference number: S00925; MUID:88122639; PMID:2893289
A;Accession: S00925
A;Molecule type: mRNA
A;Residues: 1-344,'I',365-770 <PO2>
A;Cross-references: GB:X06989; EMBL:Y00297; NID:g28720; PIDN:CAA30050.1; PID:g28721
A;Note: alternative splice form APP(751)
R;Kitaguchi, N.; Takahashi, Y.; Tokushima, Y.; Shiojiri, S.; Ito, H.
Nature 331, 530-532, 1988
A;Title: Novel precursor of Alzheimer's disease amyloid protein shows protease inhibitory activity.
A;Reference number: A38949; MUID:88122641; PMID:2893291
A;Accession: A38949
A;Molecule type: mRNA
A;Residues: 287-367 <KIT>

A;Cross-references: GB:X06981; NID:g28816; PIDN:CAA30041.1; PID:g929611
A;Experimental source: glioblastoma cell line
A;Note: alternative splice form APP(770)
R;Vitek, M.P.; Rasool, C.G.; de Sauvage, F.; Vitek, S.M.; Bartus, R.T.; Beer, B.; Ashton, R.A.; Macq, A.F.; Maloteaux, J.M.; Blume, A.J.; Octave, J.N.
Brain Res. Mol. Brain Res. 4, 121-131, 1988
A;Title: Absence of mutation in the beta-amyloid cDNAs cloned from the brains of three patients with sporadic Alzheimer's disease.
A;Reference number: A30320
A;Accession: A30320
A;Status: not compared with conceptual translation
A;Molecule type: mRNA
A;Residues: 284-288,'V',365-770 <VIT1>
A;Accession: B30320
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A;Residues: 122-288,'V',365-770 <VIT2>
A;Accession: C30320
A;Status: not compared with conceptual translation
A;Molecule type: mRNA
A;Residues: 606-770 <VIT3>
R;Zain, S.B.; Salim, M.; Chou, W.G.; Sajdel-Sulkowska, E.M.; Majocha, R.E.; Marotta, C.A.
Proc. Natl. Acad. Sci. U.S.A. 85, 929-933, 1988
A;Title: Molecular cloning of amyloid cDNA derived from mRNA of the Alzheimer disease brain: coding and noncoding regions of the fetal precursor mRNA are expressed in the cortex.
A;Reference number: A31087; MUID:88124954; PMID:2893379
A;Accession: A31087
A;Molecule type: mRNA
A;Residues: 507-770 <ZAI>
A;Cross-references: GB:M18734; NID:g178572; PIDN:AAA51726.1; PID:g178573
A;Note: the authors translated the codon GAA for residue 599 as Gly, ACC for residue 603 as Val, GTG for residue 604 as Glu, GAG for residue 605 as Leu, CTT for residue 607 as Pro, CCC for residue 608 as Val, GTG for residue 609 as Asn, AAT for residue 610 as Gly, and GGT for residue 655 as Ser
A;Note: the cited Genbank accession number, J03594, is not in release 101.0
R;Masters, C.L.; Multhaup, G.; Simms, G.; Pottgiesser, J.; Martins, R.N.; Beyreuther, K.

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Db   668 EVKMDAEF 675

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protein F13A2.1 [imported] - Caenorhabditis elegans
C;Species: Caenorhabditis elegans
C;Date: 10-May-2001 #sequence_revision 10-May-2001 #text_change 10-May-2001
C;Accession: E89026
R;anonymous, The C. elegans Sequencing Consortium.
Science 282, 2012-2018, 1998

A;Title: Genome sequence of the nematode C. elegans: a platform for investigating biology.
A;Reference number: A75000; MUID:99069613; PMID:9851916
A;Note: see websites genome.wustl.edu/gsc/C_elegans/ and www_sanger.ac.uk/Projects/C_elegans/ for a list of authors
A;Note: published errata appeared in Science 283, 35, 1999; Science 283, 2103, 1999; and Science 285, 1493, 1999
A;Accession: E89026
A;Status: preliminary
A;Molecule type: DNA
A;Residues: 1-142 <STO>
A;Cross-references: GB:chr_V; PIDN:AAB69895.1; PID:g2384795; GSPDB:GN00023; CESP:F13A2.1
C;Genetics:
A;Gene: F13A2.1
A;Map position: 5

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Qy 1 EVKMDAEF 8
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Alzheimer's disease amyloid beta protein precursor - African clawed frog
C;Species: Xenopus laevis (African clawed frog)
C;Date: 10-Jun-1993 #sequence_revision 10-Jun-1993 #text_change 13-Aug-1999
C;Accession: JH0773
R;Okado, H.; Okamoto, H.
Biochem. Biophys. Res. Commun. 189, 1561-1568, 1992
A;Title: A Xenopus homologue of the human beta-amyloid precursor protein: developmental regulation of its gene expression.
A;Reference number: JH0773; MUID:93129227; PMID:1282805
A;Accession: JH0773
A;Molecule type: mRNA
A;Residues: 1-747 <OKA>
A;Cross-references: GB:S52417; NID:g263150; PIDN:AAB24853.1; PID:g263151
A;Experimental source: larva
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C;Keywords: alternative splicing; amyloid
F;287-337/Domain: animal Kunitz-type proteinase inhibitor homology <BPI>

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Db 645 EVKMDSEY 652

RESULT 15

AF0358
conserved hypothetical protein YPO2947 [imported] - Yersinia pestis (strain CO92)
C;Species: Yersinia pestis
C;Date: 02-Nov-2001 #sequence_revision 02-Nov-2001 #text_change 23-Dec-2002
C;Accession: AF0358
R;Parkhill, J.; Wren, B.W.; Thomson, N.R.; Titball, R.W.; Holden, M.T.G.; Prentice, M.B.; Sebaihia, M.; James, K.D.; Churcher, C.; Mungall, K.L.; Baker, S.; Basham, D.; Bentley, S.D.; Brooks, K.; Cerdeno-Tarraga, A.M.; Chillingworth, T.; Cronin, A.; Davies, R.M.; Davis, P.; Dougan, G.; Feltwell, T.; Hamlin, N.; Holroyd, S.; Jagels, K.; Leather, S.; Karlyshev, A.V.; Moule, S.; Oyston, P.C.F.; Quail, M.; Rutherford, K.; Simmonds, M.; Skelton, J.; Stevens, K.; Whitehead, S.; Barrell, B.G.
Nature 413, 523-527, 2001
A;Title: Genome sequence of Yersinia pestis, the causative agent of plague.
A;Reference number: AB0001; MUID:21470413; PMID:11586360
A;Accession: AF0358
A;Status: preliminary
A;Molecule type: DNA
A;Residues: 1-626 <KUR>
A;Cross-references: GB:AL590842; PIDN:CAC92193.1; PID:g15980905; GSPDB:GN00175
C;Genetics:
A;Gene: YPO2947
C;Superfamily: uncharacterized conserved protein

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Db         61 QIKLDAEF 68
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GenCore version 5.1.6

OM protein - protein search, using sw model

Run on: January 21, 2004, 09:25:15 ; Search time 1.60612 Seconds
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1018.511 Million cell updates/sec

Title: US-09-869-414A-67
Perfect score: 40
Sequence: 1 EVKMDAEF 8

Scoring table: BLOSUM62
Gapop 10.0 , Gapext 0.5

Searched: 762491 seqs, 204481190 residues

Total number of hits satisfying chosen parameters: 762491

Minimum DB seq length: 0
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Post-processing: Minimum Match 0%
Maximum Match 100%
Listing first 45 summaries

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Pred. No. is the number of results predicted by chance to have a score greater than or equal to the score of the result being printed, and is derived by analysis of the total score distribution.

SUMMARIES

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3	40	100.0	8	9	US-09-794-743-67	Sequence 67, Appl
4	40	100.0	8	9	US-09-794-748-67	Sequence 67, Appl
5	40	100.0	8	9	US-09-794-925-67	Sequence 67, Appl
6	40	100.0	8	9	US-09-681-442-67	Sequence 67, Appl
7	40	100.0	8	11	US-09-869-414-67	Sequence 67, Appl
8	40	100.0	8	12	US-10-427-208-52	Sequence 52, Appl
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35	40	100.0	13	15	US-10-192-424-2	Sequence 2, Appli
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38	40	100.0	13	15	US-10-264-707-2	Sequence 2, Appli
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45	40	100.0	15	9	US-09-681-442-71	Sequence 71, Appl

ALIGNMENTS

RESULT 1
US-09-794-927-67
; Sequence 67, Application US/09794927
; Patent No. US20010016324A1
; GENERAL INFORMATION:
; APPLICANT: Gurney, Mark E.

; APPLICANT: Bienkowski, Michael J.
; APPLICANT: Heinrikson, Robert L.
; APPLICANT: Parodi, Luis A.
; APPLICANT: Yan, Riqiang
; TITLE OF INVENTION: ALZHEIMER'S DISEASE SECRETASE, APP SUBSTRATES THEREFOR, AND
; TITLE OF INVENTION: USES
; TITLE OF INVENTION: THEREFOR
; FILE REFERENCE: 28341/6280FG
; CURRENT APPLICATION NUMBER: US/09/794,927
; CURRENT FILING DATE: 2001-02-27
; PRIOR APPLICATION NUMBER: 09/416,901
; PRIOR FILING DATE: 1999-10-13
; PRIOR APPLICATION NUMBER: 60/155,493
; PRIOR FILING DATE: 1999-09-23
; PRIOR APPLICATION NUMBER: 09/404,133
; PRIOR FILING DATE: 1999-09-23
; PRIOR APPLICATION NUMBER: PCT/US99/20881
; PRIOR FILING DATE: 1999-09-23
; PRIOR APPLICATION NUMBER: 60/101,594
; PRIOR FILING DATE: 1998-09-24
; NUMBER OF SEQ ID NOS: 73
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; ORGANISM: Artificial Sequence
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; OTHER INFORMATION: Description of Artificial Sequence: Peptide
US-09-794-927-67

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Db 1 EVKMDAEF 8

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; Patent No. US20010018208A1
; GENERAL INFORMATION:
; APPLICANT: Gurney, Mark E.
; APPLICANT: Bienkowski, Michael J.
; APPLICANT: Heinrikson, Robert L.
; APPLICANT: Parodi, Luis A.
; APPLICANT: Yan, Riqiang
; TITLE OF INVENTION: ALZHEIMER'S DISEASE SECRETASE, APP SUBSTRATES THEREFOR, AND
; TITLE OF INVENTION: USES
; TITLE OF INVENTION: THEREFOR
; FILE REFERENCE: 28341/6280DE
; CURRENT APPLICATION NUMBER: US/09/795,847
; CURRENT FILING DATE: 2001-02-28

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;  PRIOR FILING DATE:  1999-09-23
;  PRIOR APPLICATION NUMBER:  09/404,133
;  PRIOR FILING DATE:  1999-09-23
;  PRIOR APPLICATION NUMBER:  PCT/US99/20881
;  PRIOR FILING DATE:  1999-09-23
;  PRIOR APPLICATION NUMBER:  60/101,594
;  PRIOR FILING DATE:  1998-09-24
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;   OTHER INFORMATION: Description of Artificial Sequence: Peptide
US-09-795-847-67

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Db          1 EVKMDAEF 8


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; GENERAL INFORMATION:
;  APPLICANT:  Gurney, Mark E.
;  APPLICANT:  Bienkowski, Michael J.
;  APPLICANT:  Heinrikson, Robert L.
;  APPLICANT:  Parodi, Luis A.
;  APPLICANT:  Yan, Riqiang
;  TITLE OF INVENTION:  ALZHEIMER'S DISEASE SECRETASE, APP SUBSTRATES THEREFOR,
AND
;  TITLE OF INVENTION:  USES
;  TITLE OF INVENTION:  THEREFOR
;  FILE REFERENCE:  28341/6280BC
;  CURRENT APPLICATION NUMBER: US/09/794,743
;  CURRENT FILING DATE:  2001-02-27
;  PRIOR APPLICATION NUMBER:  09/416,901
;  PRIOR FILING DATE:  1999-10-13
;  PRIOR APPLICATION NUMBER:  60/155,493
;  PRIOR FILING DATE:  1999-09-23
;  PRIOR APPLICATION NUMBER:  09/404,133
;  PRIOR FILING DATE:  1999-09-23
;  PRIOR APPLICATION NUMBER:  PCT/US99/20881
;  PRIOR FILING DATE:  1999-09-23
;  PRIOR APPLICATION NUMBER:  60/101,594
;  PRIOR FILING DATE:  1998-09-24
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; SOFTWARE: PatentIn Ver. 2.0
; SEQ ID NO 67
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; OTHER INFORMATION: Description of Artificial Sequence: Peptide
US-09-794-743-67

Query Match 100.0%; Score 40; DB 9; Length 8;
Best Local Similarity 100.0%; Pred. No. 6.7e+05;
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; APPLICANT: Gurney, Mark E.
; APPLICANT: Bienkowski, Michael J.
; APPLICANT: Heinrikson, Robert L.
; APPLICANT: Parodi, Luis A.
; APPLICANT: Yan, Riqiang
; TITLE OF INVENTION: ALZHEIMER'S DISEASE SECRETASE, APP SUBSTRATES THEREFOR, AND
; TITLE OF INVENTION: USES
; TITLE OF INVENTION: THEREFOR
; FILE REFERENCE: 28341/6280JL
; CURRENT APPLICATION NUMBER: US/09/794,748
; CURRENT FILING DATE: 2001-02-27
; PRIOR APPLICATION NUMBER: 09/416,901
; PRIOR FILING DATE: 1999-10-13
; PRIOR APPLICATION NUMBER: 60/155,493
; PRIOR FILING DATE: 1999-09-23
; PRIOR APPLICATION NUMBER: 09/404,133
; PRIOR FILING DATE: 1999-09-23
; PRIOR APPLICATION NUMBER: PCT/US99/20881
; PRIOR FILING DATE: 1999-09-23
; PRIOR APPLICATION NUMBER: 60/101,594
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US-09-794-748-67

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RESULT 5
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; Patent No. US20020064819A1
; GENERAL INFORMATION:
; APPLICANT: Gurney, Mark E.
; APPLICANT: Bienkowski, Michael J.
; APPLICANT: Heinrikson, Robert L.
; APPLICANT: Parodi, Luis A.
; APPLICANT: Yan, Riqiang
; TITLE OF INVENTION: ALZHEIMER'S DISEASE SECRETASE, APP SUBSTRATES THEREFOR, AND USES
; TITLE OF INVENTION: THEREFOR
; FILE REFERENCE: 28341/6280HI
; CURRENT APPLICATION NUMBER: US/09/794,925
; CURRENT FILING DATE: 2001-02-27
; PRIOR APPLICATION NUMBER: 09/416,901
; PRIOR FILING DATE: 1999-10-13
; PRIOR APPLICATION NUMBER: 60/155,493
; PRIOR FILING DATE: 1999-09-23
; PRIOR APPLICATION NUMBER: 09/404,133
; PRIOR FILING DATE: 1999-09-23
; PRIOR APPLICATION NUMBER: PCT/US99/20881
; PRIOR FILING DATE: 1999-09-23
; PRIOR APPLICATION NUMBER: 60/101,594
; PRIOR FILING DATE: 1998-09-24
; NUMBER OF SEQ ID NOS: 73
; SOFTWARE: PatentIn Ver. 2.0
; SEQ ID NO 67
; LENGTH: 8
; TYPE: PRT
; ORGANISM: Artificial Sequence
; FEATURE:
; OTHER INFORMATION: Description of Artificial Sequence: Peptide
US-09-794-925-67

Query Match 100.0%; Score 40; DB 9; Length 8;
Best Local Similarity 100.0%; Pred. No. 6.7e+05;
Matches 8; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

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Qy          1 EVKMDAEF 8
              ||||||||
Db          1 EVKMDAEF 8
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RESULT 6
US-09-681-442-67
; Sequence 67, Application US/09681442
; Patent No. US20020081634A1
; GENERAL INFORMATION:

; APPLICANT: Gurney, Mark E.
; APPLICANT: Bienkowski, Michael J.
; APPLICANT: Heinrikson, Robert L.
; APPLICANT: Parodi, Luis A.
; APPLICANT: Yan, Riqiang
; TITLE OF INVENTION: ALZHEIMER'S DISEASE SECRETASE, APP SUBSTRATES THEREFOR, AND USES
; TITLE OF INVENTION: THEREFOR
; FILE REFERENCE: 28341/6280FG
; CURRENT APPLICATION NUMBER: US/09/681,442
; CURRENT FILING DATE: 2001-04-05
; PRIOR APPLICATION NUMBER: 09/416,901
; PRIOR FILING DATE: 1999-10-13
; PRIOR APPLICATION NUMBER: 60/155,493
; PRIOR FILING DATE: 1999-09-23
; PRIOR APPLICATION NUMBER: 09/404,133
; PRIOR FILING DATE: 1999-09-23
; PRIOR APPLICATION NUMBER: PCT/US99/20881
; PRIOR FILING DATE: 1999-09-23
; PRIOR APPLICATION NUMBER: 60/101,594
; PRIOR FILING DATE: 1998-09-24
; NUMBER OF SEQ ID NOS: 73
; SOFTWARE: PatentIn Ver. 2.0
; SEQ ID NO 67
; LENGTH: 8
; TYPE: PRT
; ORGANISM: Artificial Sequence
; FEATURE:
; OTHER INFORMATION: Description of Artificial Sequence: Peptide
US-09-681-442-67

Query Match 100.0%; Score 40; DB 9; Length 8;
Best Local Similarity 100.0%; Pred. No. 6.7e+05;
Matches 8; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

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Qy          1 EVKMDAEF 8
              ||||||||
Db          1 EVKMDAEF 8
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RESULT 7
US-09-869-414-67
; Sequence 67, Application US/09869414
; Publication No. US20030077226A1
; GENERAL INFORMATION:
; APPLICANT: Beinkowski et al.
; TITLE OF INVENTION: ALZHEIMER'S DISEASE SECRETASE, APP SUBSTRATES THEREFOR, AND USES
; TITLE OF INVENTION: THEREFOR
; FILE REFERENCE: 28341/6280M
; CURRENT APPLICATION NUMBER: US/09/869,414
; CURRENT FILING DATE: 2001-06-27
; PRIOR APPLICATION NUMBER: 09/416,901
; PRIOR FILING DATE: 1999-10-13
; PRIOR APPLICATION NUMBER: 60/155,493
; PRIOR FILING DATE: 1999-09-23
; PRIOR APPLICATION NUMBER: 09/404,133

; PRIOR FILING DATE: 1999-09-23
; PRIOR APPLICATION NUMBER: PCT/US99/20881
; PRIOR FILING DATE: 1999-09-23
; PRIOR APPLICATION NUMBER: 60/101,594
; PRIOR FILING DATE: 1998-09-24
; NUMBER OF SEQ ID NOS: 73
; SOFTWARE: PatentIn Ver. 2.0
; SEQ ID NO 67
;   LENGTH: 8
;   TYPE: PRT
;   ORGANISM: Artificial Sequence
;   FEATURE:
;   OTHER INFORMATION: Description of Artificial Sequence: Peptide
US-09-869-414-67

  Query Match   100.0%; Score 40; DB 11; Length 8;
  Best Local Similarity   100.0%; Pred. No. 6.7e+05;
  Matches   8; Conservative   0; Mismatches   0; Indels   0; Gaps   0;

Qy   1 EVKMDAEF 8
              ||||||||
Db   1 EVKMDAEF 8

RESULT 8
US-10-427-208-52
; Sequence 52, Application US/10427208
; Publication No. US20030200555A1
; GENERAL INFORMATION:
; APPLICANT: Merck & Co., Inc.
; APPLICANT: Hazuda, Daria J
; APPLICANT: Chen Dodson, Elizabeth
; APPLICANT: Lai, Ming-Tain
; APPLICANT: Xu, Min
; APPLICANT: Shi, Xiao-Ping
; APPLICANT: Simon, Adam J.
; APPLICANT: Wu, Guoxin
; APPLICANT: Li, Yueming
; APPLICANT: Register, Robert B.
; TITLE OF INVENTION: ASSAYS USING AMYLOID PRECURSOR PROTEINS WITH MODIFIED
; TITLE OF INVENTION: BETA-SECRETASE CLEAVAGE SITES TO MONITOR BETA-SECRETASE
ACTIVITY
; FILE REFERENCE: 21052
; CURRENT APPLICATION NUMBER: US/10/427,208
; CURRENT FILING DATE: 2003-04-30
; NUMBER OF SEQ ID NOS: 75
; SOFTWARE: PatentIn version 3.2
; SEQ ID NO 52
;   LENGTH: 8
;   TYPE: PRT
;   ORGANISM: Homo sapiens
US-10-427-208-52

  Query Match   100.0%; Score 40; DB 12; Length 8;
  Best Local Similarity   100.0%; Pred. No. 6.7e+05;
  Matches   8; Conservative   0; Mismatches   0; Indels   0; Gaps   0;

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Qy          1 EVKMDAEF 8
              ||||||||
Db          1 EVKMDAEF 8


RESULT 9
US-10-066-319-3
; Sequence 3, Application US/10066319
; Publication No. US20030147810A1
; GENERAL INFORMATION:
;  APPLICANT: Ross, Brian D.
;  APPLICANT:  Rehemtulla, Alnawaz
;  TITLE OF INVENTION: COMPOSITIONS AND METHODS FOR REPORTING
;  TITLE OF INVENTION:  OF PROTEASE ACTIVITY WITHIN THE SECRETORY PATHWAY
;  FILE REFERENCE: 11203-007001
;  CURRENT APPLICATION NUMBER: US/10/066,319
;  CURRENT FILING DATE:  2002-06-17
;  NUMBER OF SEQ ID NOS: 18
;  SOFTWARE: FastSEQ for Windows Version 4.0
; SEQ ID NO 3
;   LENGTH: 9
;   TYPE: PRT
;   ORGANISM: Homo sapiens
US-10-066-319-3

  Query Match             100.0%;  Score 40;  DB 12;  Length 9;
  Best Local Similarity   100.0%;  Pred. No. 6.7e+05;
  Matches    8;  Conservative    0;  Mismatches    0;  Indels    0;  Gaps    0;

Qy          1 EVKMDAEF 8
              ||||||||
Db          2 EVKMDAEF 9


RESULT 10
US-10-016-717-6
; Sequence 6, Application US/10016717
; Publication No. US20020132281A1
; GENERAL INFORMATION:
;  APPLICANT: Hook, Vivian Y.H.
;  TITLE OF INVENTION: SECRETASES RELATED TO ALZHEIMER'S DEMENTIA
;  FILE REFERENCE: P-AS 5031
;  CURRENT APPLICATION NUMBER: US/10/016,717
;  CURRENT FILING DATE:  2002-03-12
;  PRIOR APPLICATION NUMBER: US 09/173,887
;  PRIOR FILING DATE: 1998-10-16
;  PRIOR APPLICATION NUMBER: US 09/294,987
;  PRIOR FILING DATE: 1999-04-20
;  NUMBER OF SEQ ID NOS: 6
;  SOFTWARE: PatentIn Ver. 2.0
; SEQ ID NO 6
;   LENGTH: 9
;   TYPE: PRT
;   ORGANISM: mammalian
US-10-016-717-6

  Query Match             100.0%;  Score 40;  DB 14;  Length 9;
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  Best Local Similarity   100.0%;  Pred. No. 6.7e+05;
  Matches    8;  Conservative    0;  Mismatches    0;  Indels    0;  Gaps    0;

Qy          1 EVKMDAEF 8
              ||||||||
Db          2 EVKMDAEF 9


RESULT 11
US-09-794-927-64
; Sequence 64, Application US/09794927
; Patent No. US20010016324A1
; GENERAL INFORMATION:
;  APPLICANT:  Gurney, Mark E.
;  APPLICANT:  Bienkowski, Michael J.
;  APPLICANT:  Heinrikson, Robert L.
;  APPLICANT:  Parodi, Luis A.
;  APPLICANT:  Yan, Riqiang
;  TITLE OF INVENTION:  ALZHEIMER'S DISEASE SECRETASE, APP SUBSTRATES THEREFOR,
AND
;  TITLE OF INVENTION:  USES
;  TITLE OF INVENTION:  THEREFOR
;  FILE REFERENCE:  28341/6280FG
;  CURRENT APPLICATION NUMBER: US/09/794,927
;  CURRENT FILING DATE:  2001-02-27
;  PRIOR APPLICATION NUMBER:  09/416,901
;  PRIOR FILING DATE:  1999-10-13
;  PRIOR APPLICATION NUMBER:  60/155,493
;  PRIOR FILING DATE:  1999-09-23
;  PRIOR APPLICATION NUMBER:  09/404,133
;  PRIOR FILING DATE:  1999-09-23
;  PRIOR APPLICATION NUMBER:  PCT/US99/20881
;  PRIOR FILING DATE:  1999-09-23
;  PRIOR APPLICATION NUMBER:  60/101,594
;  PRIOR FILING DATE:  1998-09-24
;  NUMBER OF SEQ ID NOS:  73
;  SOFTWARE:  PatentIn Ver. 2.0
; SEQ ID NO 64
;   LENGTH: 10
;   TYPE: PRT
;   ORGANISM: Artificial Sequence
;   FEATURE:
;   OTHER INFORMATION: Description of Artificial Sequence: synthetic
US-09-794-927-64

  Query Match             100.0%;  Score 40;  DB 9;  Length 10;
  Best Local Similarity   100.0%;  Pred. No. 0.041;
  Matches    8;  Conservative    0;  Mismatches    0;  Indels    0;  Gaps    0;

Qy          1 EVKMDAEF 8
              ||||||||
Db          2 EVKMDAEF 9


RESULT 12
US-09-795-847-64
; Sequence 64, Application US/09795847
```

; Patent No. US20010018208A1
; GENERAL INFORMATION:
; APPLICANT: Gurney, Mark E.
; APPLICANT: Bienkowski, Michael J.
; APPLICANT: Heinrikson, Robert L.
; APPLICANT: Parodi, Luis A.
; APPLICANT: Yan, Riqiang
; TITLE OF INVENTION: ALZHEIMER'S DISEASE SECRETASE, APP SUBSTRATES THEREFOR, AND
; TITLE OF INVENTION: USES
; TITLE OF INVENTION: THEREFOR
; FILE REFERENCE: 28341/6280DE
; CURRENT APPLICATION NUMBER: US/09/795,847
; CURRENT FILING DATE: 2001-02-28
; PRIOR APPLICATION NUMBER: 09/416,901
; PRIOR FILING DATE: 1999-10-13
; PRIOR APPLICATION NUMBER: 60/155,493
; PRIOR FILING DATE: 1999-09-23
; PRIOR APPLICATION NUMBER: 09/404,133
; PRIOR FILING DATE: 1999-09-23
; PRIOR APPLICATION NUMBER: PCT/US99/20881
; PRIOR FILING DATE: 1999-09-23
; PRIOR APPLICATION NUMBER: 60/101,594
; PRIOR FILING DATE: 1998-09-24
; NUMBER OF SEQ ID NOS: 73
; SOFTWARE: PatentIn Ver. 2.0
; SEQ ID NO 64
; LENGTH: 10
; TYPE: PRT
; ORGANISM: Artificial Sequence
; FEATURE:
; OTHER INFORMATION: Description of Artificial Sequence: synthetic
US-09-795-847-64

Query Match 100.0%; Score 40; DB 9; Length 10;
Best Local Similarity 100.0%; Pred. No. 0.041;
Matches 8; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

Qy 1 EVKMDAEF 8
||||||||
Db 2 EVKMDAEF 9

RESULT 13
US-09-794-743-64
; Sequence 64, Application US/09794743
; Patent No. US20010021391A1
; GENERAL INFORMATION:
; APPLICANT: Gurney, Mark E.
; APPLICANT: Bienkowski, Michael J.
; APPLICANT: Heinrikson, Robert L.
; APPLICANT: Parodi, Luis A.
; APPLICANT: Yan, Riqiang
; TITLE OF INVENTION: ALZHEIMER'S DISEASE SECRETASE, APP SUBSTRATES THEREFOR, AND
; TITLE OF INVENTION: USES
; TITLE OF INVENTION: THEREFOR

; FILE REFERENCE: 28341/6280BC
; CURRENT APPLICATION NUMBER: US/09/794,743
; CURRENT FILING DATE: 2001-02-27
; PRIOR APPLICATION NUMBER: 09/416,901
; PRIOR FILING DATE: 1999-10-13
; PRIOR APPLICATION NUMBER: 60/155,493
; PRIOR FILING DATE: 1999-09-23
; PRIOR APPLICATION NUMBER: 09/404,133
; PRIOR FILING DATE: 1999-09-23
; PRIOR APPLICATION NUMBER: PCT/US99/20881
; PRIOR FILING DATE: 1999-09-23
; PRIOR APPLICATION NUMBER: 60/101,594
; PRIOR FILING DATE: 1998-09-24
; NUMBER OF SEQ ID NOS: 73
; SOFTWARE: PatentIn Ver. 2.0
; SEQ ID NO 64
;   LENGTH: 10
;   TYPE: PRT
;   ORGANISM: Artificial Sequence
;   FEATURE:
;   OTHER INFORMATION: Description of Artificial Sequence: synthetic
US-09-794-743-64

  Query Match   100.0%; Score 40; DB 9; Length 10;
  Best Local Similarity 100.0%; Pred. No. 0.041;
  Matches   8; Conservative   0; Mismatches   0; Indels   0; Gaps   0;

Qy   1 EVKMDAEF 8
              ||||||||
Db   2 EVKMDAEF 9

RESULT 14
US-09-794-748-64
; Sequence 64, Application US/09794748
; Patent No. US20020037315A1
; GENERAL INFORMATION:
; APPLICANT: Gurney, Mark E.
; APPLICANT: Bienkowski, Michael J.
; APPLICANT: Heinrikson, Robert L.
; APPLICANT: Parodi, Luis A.
; APPLICANT: Yan, Riqiang
; TITLE OF INVENTION: ALZHEIMER'S DISEASE SECRETASE, APP SUBSTRATES THEREFOR,
AND
; TITLE OF INVENTION: USES
; TITLE OF INVENTION: THEREFOR
; FILE REFERENCE: 28341/6280JL
; CURRENT APPLICATION NUMBER: US/09/794,748
; CURRENT FILING DATE: 2001-02-27
; PRIOR APPLICATION NUMBER: 09/416,901
; PRIOR FILING DATE: 1999-10-13
; PRIOR APPLICATION NUMBER: 60/155,493
; PRIOR FILING DATE: 1999-09-23
; PRIOR APPLICATION NUMBER: 09/404,133
; PRIOR FILING DATE: 1999-09-23
; PRIOR APPLICATION NUMBER: PCT/US99/20881
; PRIOR FILING DATE: 1999-09-23

; PRIOR APPLICATION NUMBER: 60/101,594
; PRIOR FILING DATE: 1998-09-24
; NUMBER OF SEQ ID NOS: 73
; SOFTWARE: PatentIn Ver. 2.0
; SEQ ID NO 64
;   LENGTH: 10
;   TYPE: PRT
;   ORGANISM: Artificial Sequence
;   FEATURE:
;   OTHER INFORMATION: Description of Artificial Sequence: synthetic
US-09-794-748-64

  Query Match   100.0%; Score 40; DB 9; Length 10;
  Best Local Similarity   100.0%; Pred. No. 0.041;
  Matches   8; Conservative   0; Mismatches   0; Indels   0; Gaps   0;

Qy   1 EVKMDAEF 8
              ||||||||
Db   2 EVKMDAEF 9

RESULT 15
US-09-796-264-4
; Sequence 4, Application US/09796264
; Patent No. US20020049303A1
; GENERAL INFORMATION:
; APPLICANT: Tang, Jordan J.N.
; APPLICANT: Lin, Xinli
; APPLICANT: Koelsch, Gerald
; TITLE OF INVENTION: Catalytically Active Recombinant Memapsin and Methods
; TITLE OF INVENTION: of Use Thereof
; FILE REFERENCE: OMRF 179
; CURRENT APPLICATION NUMBER: US/09/796,264
; CURRENT FILING DATE: 2001-02-28
; PRIOR APPLICATION NUMBER: 09/604,608
; PRIOR FILING DATE: 2000-06-27
; PRIOR APPLICATION NUMBER: 60/168,060
; PRIOR FILING DATE: 1999-11-30
; PRIOR APPLICATION NUMBER: 60/177,836
; PRIOR FILING DATE: 2000-01-25
; PRIOR APPLICATION NUMBER: 60/178,368
; PRIOR FILING DATE: 2000-01-27
; PRIOR APPLICATION NUMBER: 60/210,292
; PRIOR FILING DATE: 2000-06-08
; NUMBER OF SEQ ID NOS: 31
; SOFTWARE: PatentIn Ver. 2.1
; SEQ ID NO 4
;   LENGTH: 10
;   TYPE: PRT
;   ORGANISM: Artificial Sequence
;   FEATURE:
;   OTHER INFORMATION: Description of Artificial Sequence: Primer
US-09-796-264-4

  Query Match   100.0%; Score 40; DB 9; Length 10;
  Best Local Similarity   100.0%; Pred. No. 0.041;
  Matches   8; Conservative   0; Mismatches   0; Indels   0; Gaps   0;

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Qy          1 EVKMDAEF 8
              ||||||||
Db          2 EVKMDAEF 9
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Search completed: January 21, 2004, 09:41:42
Job time : 1.60612 secs

GenCore version 5.1.6

OM protein - protein search, using sw model

Run on: January 21, 2004, 09:16:19 ; Search time 1.65201 Seconds
(without alignments)
1249.644 Million cell updates/sec

Title: US-09-869-414A-67
Perfect score: 40
Sequence: 1 EVKMDAEF 8

Scoring table: BLOSUM62
Gapop 10.0 , Gapext 0.5

Searched: 830525 seqs, 258052604 residues

Total number of hits satisfying chosen parameters: 830525

Minimum DB seq length: 0
Maximum DB seq length: 2000000000

Post-processing: Minimum Match 0%
Maximum Match 100%
Listing first 45 summaries

Database : SPTREMBL_23:*
1: sp_archea:*
2: sp_bacteria:*
3: sp_fungi:*
4: sp_human:*
5: sp_invertebrate:*
6: sp_mammal:*
7: sp_mhc:*
8: sp_organelle:*
9: sp_phage:*
10: sp_plant:*
11: sp_rodent:*
12: sp_virus:*
13: sp_vertebrate:*
14: sp_unclassified:*
15: sp_rvirus:*
16: sp_bacteriap:*
17: sp_archeap:*

Pred. No. is the number of results predicted by chance to have a score greater than or equal to the score of the result being printed, and is derived by analysis of the total score distribution.

SUMMARIES

Result No.	Score	% Query Match	Length	DB	ID	Description

1	40	100.0	35	4	Q8WZ99	Q8wz99 homo sapien
2	40	100.0	79	11	O35463	O35463 cricetulus
3	40	100.0	82	4	Q16020	Q16020 homo sapien
4	40	100.0	82	4	Q16014	Q16014 homo sapien
5	40	100.0	82	4	Q16019	Q16019 homo sapien
6	40	100.0	113	13	Q8JH58	Q8jh58 chelydra se
7	40	100.0	218	11	Q8BPV5	Q8bpv5 mus musculu
8	40	100.0	384	11	Q8BPC7	Q8bpc7 mus musculu
9	40	100.0	534	13	O93296	O93296 gallus gall
10	40	100.0	569	13	Q9PVL1	Q9pvl1 gallus gall
11	40	100.0	607	11	Q99K32	Q99k32 mus musculu
12	40	100.0	695	11	Q60496	Q60496 cavia sp. p
13	40	100.0	695	11	P97487	P97487 mus musculu
14	40	100.0	695	13	Q9DGJ8	Q9dgj8 gallus gall
15	40	100.0	751	13	Q9DGJ7	Q9dgj7 gallus gall
16	40	100.0	770	6	Q9TUI0	Q9tui0 sus scrofa
17	35	87.5	2148	5	Q8IPL5	Q8ipl5 drosophila
18	34	85.0	142	5	O16896	O16896 caenorhabdi
19	34	85.0	693	13	Q98SG0	Q98sg0 xenopus lae
20	34	85.0	695	13	Q98SF9	Q98sf9 xenopus lae
21	34	85.0	747	13	Q91963	Q91963 xenopus. ap
22	33	82.5	317	17	Q96ZT2	Q96zt2 sulfolobus
23	33	82.5	423	2	O52379	O52379 ralstonia s
24	33	82.5	423	2	Q45693	Q45693 burkholderi
25	33	82.5	626	16	Q8ZCN4	Q8zcn4 yersinia pe
26	32	80.0	286	2	Q8VNV1	Q8vnv1 chlorobium
27	32	80.0	289	2	Q8VNV3	Q8vnv3 chlorobium
28	32	80.0	289	2	Q8VNW1	Q8vnw1 chlorobium
29	32	80.0	289	2	Q8VNV2	Q8vnv2 chlorobium
30	32	80.0	289	2	Q8VL89	Q8vl89 chlorobium
31	32	80.0	289	2	Q8VLL7	Q8vll7 chlorobium
32	32	80.0	338	2	Q9AL67	Q9al67 chlorobium
33	32	80.0	350	2	Q9AL73	Q9al73 chlorobium
34	32	80.0	350	2	Q9AL69	Q9al69 chlorobium
35	32	80.0	350	2	Q9AL72	Q9al72 chlorobium
36	32	80.0	426	17	Q9V2P8	Q9v2p8 pyrococcus
37	32	80.0	630	2	Q93IK4	Q93ik4 vibrio sp.
38	32	80.0	859	3	Q9HFI9	Q9hfi9 neurospora
39	31	77.5	119	17	Q8ZZP0	Q8zzp0 pyrobaculum
40	31	77.5	161	16	Q98FZ2	Q98fz2 rhizobium l
41	31	77.5	282	5	O02335	O02335 caenorhabdi
42	31	77.5	328	11	Q9CZC7	Q9czc7 mus musculu
43	31	77.5	328	11	Q8BPI1	Q8bpi1 mus musculu
44	31	77.5	705	16	Q8E8V4	Q8e8v4 shewanella
45	31	77.5	1209	10	Q94FG7	Q94fg7 chlamydomon

ALIGNMENTS

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RESULT 1
Q8WZ99
ID   Q8WZ99      PRELIMINARY;      PRT;    35 AA.
AC   Q8WZ99;
DT   01-MAR-2002 (TrEMBLrel. 20, Created)
DT   01-MAR-2002 (TrEMBLrel. 20, Last sequence update)
DT   01-MAR-2002 (TrEMBLrel. 20, Last annotation update)
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DE   Amyloid protein (Fragment).
GN   APP.
OS   Homo sapiens (Human).
OC   Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
OC   Mammalia; Eutheria; Primates; Catarrhini; Hominidae; Homo.
OX   NCBI_TaxID=9606;
RN   [1]
RP   SEQUENCE FROM N.A.
RA   Wakutani Y., Ninomiya H., Iwata H., Tanaka S., Urakami K., Adachi Y.,
RA   Wada-Isoe K., Yamagata K., Ohono K., Tsubuki S., Saido T.,
RA   Hashimoto T., Iwatsubo T., Nakashima K.;
RT   "Novel missense mutation (D678N) of amyloid precursor protein gene in
RT   a Japanese pedigree of familial Alzheimer's disease.";
RL   Submitted (JUL-2001) to the EMBL/GenBank/DDBJ databases.
DR   EMBL; AB066441; BAB71958.1; -.
FT   NON_TER       1      1
FT   NON_TER      35     35
SQ   SEQUENCE   35 AA;  4084 MW;  49D7D17289743B71 CRC64;

  Query Match             100.0%;  Score 40;  DB 4;  Length 35;
  Best Local Similarity   100.0%;  Pred. No. 0.14;
  Matches    8;  Conservative    0;  Mismatches    0;  Indels    0;  Gaps    0;

Qy          1 EVKMDAEF 8
              ||||||||
Db         13 EVKMDAEF 20


RESULT 2
O35463
ID   O35463      PRELIMINARY;      PRT;    79 AA.
AC   O35463;
DT   01-JAN-1998 (TrEMBLrel. 05, Created)
DT   01-JAN-1998 (TrEMBLrel. 05, Last sequence update)
DT   01-JUN-2002 (TrEMBLrel. 21, Last annotation update)
DE   Alzheimer's amyloid beta protein (Fragment).
GN   BETA APP.
OS   Cricetulus griseus (Chinese hamster).
OC   Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
OC   Mammalia; Eutheria; Rodentia; Sciurognathi; Muridae; Cricetinae;
OC   Cricetulus.
OX   NCBI_TaxID=10029;
RN   [1]
RP   SEQUENCE FROM N.A.
RA   Sambamurti K., Pinnix I., Gandhi S.;
RL   Submitted (OCT-1997) to the EMBL/GenBank/DDBJ databases.
DR   EMBL; AF030413; AAB86608.1; -.
DR   HSSP; P05067; 1BA4.
DR   InterPro; IPR001255; Beta-APP.
DR   Pfam; PF03494; Beta-APP; 1.
FT   NON_TER       1      1
FT   NON_TER      79     79
SQ   SEQUENCE   79 AA;  8538 MW;  37F2C6C3BFF3F597 CRC64;

  Query Match             100.0%;  Score 40;  DB 11;  Length 79;
  Best Local Similarity   100.0%;  Pred. No. 0.31;
  Matches    8;  Conservative    0;  Mismatches    0;  Indels    0;  Gaps    0;
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Qy          1 EVKMDAEF 8
              ||||||||
Db         17 EVKMDAEF 24


RESULT 3
Q16020
ID   Q16020      PRELIMINARY;      PRT;    82 AA.
AC   Q16020;
DT   01-NOV-1996 (TrEMBLrel. 01, Created)
DT   01-NOV-1996 (TrEMBLrel. 01, Last sequence update)
DT   01-JUN-2002 (TrEMBLrel. 21, Last annotation update)
DE   Beta-amyloid peptide (Fragment).
GN   BETA APP.
OS   Homo sapiens (Human).
OC   Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
OC   Mammalia; Eutheria; Primates; Catarrhini; Hominidae; Homo.
OX   NCBI_TaxID=9606;
RN   [1]
RP   SEQUENCE FROM N.A.
RX   MEDLINE=93236601; PubMed=8476439;
RA   Denman R.B., Rosenzcwaig R., Miller D.L.;
RT   "A system for studying the effect(s) of familial Alzheimer disease
RT   mutations on the processing of the beta-amyloid peptide precursor.";
RL   Biochem. Biophys. Res. Commun. 192:96-103(1993).
DR   EMBL; S61383; AAB26265.2; -.
DR   HSSP; P05067; 1BA4.
DR   InterPro; IPR001255; Beta-APP.
DR   Pfam; PF03494; Beta-APP; 1.
FT   NON_TER       1      1
FT   NON_TER      82     82
SQ   SEQUENCE   82 AA;  8882 MW;  F534AA5AE5D9230A CRC64;

  Query Match             100.0%;  Score 40;  DB 4;  Length 82;
  Best Local Similarity   100.0%;  Pred. No. 0.32;
  Matches    8;  Conservative    0;  Mismatches    0;  Indels    0;  Gaps    0;

Qy          1 EVKMDAEF 8
              ||||||||
Db         14 EVKMDAEF 21


RESULT 4
Q16014
ID   Q16014      PRELIMINARY;      PRT;    82 AA.
AC   Q16014;
DT   01-NOV-1996 (TrEMBLrel. 01, Created)
DT   01-NOV-1996 (TrEMBLrel. 01, Last sequence update)
DT   01-JUN-2002 (TrEMBLrel. 21, Last annotation update)
DE   Beta-amyloid peptide (Fragment).
OS   Homo sapiens (Human).
OC   Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
OC   Mammalia; Eutheria; Primates; Catarrhini; Hominidae; Homo.
OX   NCBI_TaxID=9606;
RN   [1]
RP   SEQUENCE FROM N.A.
```

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RX   MEDLINE=93236601; PubMed=8476439;
RA   Denman R.B., Rosenzcwaig R., Miller D.L.;
RT   "A system for studying the effect(s) of familial Alzheimer disease
RT   mutations on the processing of the beta-amyloid peptide precursor.";
RL   Biochem. Biophys. Res. Commun. 192:96-103(1993).
DR   EMBL; S60721; AAB26263.2; -.
DR   HSSP; P05067; 1BA4.
DR   InterPro; IPR001255; Beta-APP.
DR   Pfam; PF03494; Beta-APP; 1.
FT   NON_TER       1      1
FT   NON_TER      82     82
SQ   SEQUENCE   82 AA;  8972 MW;  F534AA5B3EA9230A CRC64;

  Query Match             100.0%;  Score 40;  DB 4;  Length 82;
  Best Local Similarity   100.0%;  Pred. No. 0.32;
  Matches    8;  Conservative    0;  Mismatches    0;  Indels    0;  Gaps    0;

Qy          1 EVKMDAEF 8
              ||||||||
Db         14 EVKMDAEF 21


RESULT 5
Q16019
ID   Q16019      PRELIMINARY;      PRT;    82 AA.
AC   Q16019;
DT   01-NOV-1996 (TrEMBLrel. 01, Created)
DT   01-NOV-1996 (TrEMBLrel. 01, Last sequence update)
DT   01-JUN-2002 (TrEMBLrel. 21, Last annotation update)
DE   Beta-amyloid peptide (Fragment).
GN   BETA APP.
OS   Homo sapiens (Human).
OC   Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
OC   Mammalia; Eutheria; Primates; Catarrhini; Hominidae; Homo.
OX   NCBI_TaxID=9606;
RN   [1]
RP   SEQUENCE FROM N.A.
RX   MEDLINE=93236601; PubMed=8476439;
RA   Denman R.B., Rosenzcwaig R., Miller D.L.;
RT   "A system for studying the effect(s) of familial Alzheimer disease
RT   mutations on the processing of the beta-amyloid peptide precursor.";
RL   Biochem. Biophys. Res. Commun. 192:96-103(1993).
DR   EMBL; S61380; AAB26264.2; -.
DR   HSSP; P05067; 1BA4.
DR   InterPro; IPR001255; Beta-APP.
DR   Pfam; PF03494; Beta-APP; 1.
FT   NON_TER       1      1
FT   NON_TER      82     82
SQ   SEQUENCE   82 AA;  8938 MW;  F534AA50E579230A CRC64;

  Query Match             100.0%;  Score 40;  DB 4;  Length 82;
  Best Local Similarity   100.0%;  Pred. No. 0.32;
  Matches    8;  Conservative    0;  Mismatches    0;  Indels    0;  Gaps    0;

Qy          1 EVKMDAEF 8
              ||||||||
Db         14 EVKMDAEF 21
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RESULT 6
Q8JH58
ID   Q8JH58      PRELIMINARY;      PRT;   113 AA.
AC   Q8JH58;
DT   01-OCT-2002 (TrEMBLrel. 22, Created)
DT   01-OCT-2002 (TrEMBLrel. 22, Last sequence update)
DT   01-MAR-2003 (TrEMBLrel. 23, Last annotation update)
DE   Amyloid beta protein (Fragment).
OS   Chelydra serpentina serpentina (common snapping turtle).
OC   Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
OC   Testudines; Cryptodira; Testudinoidea; Chelydridae; Chelydra.
OX   NCBI_TaxID=134619;
RN   [1]
RP   SEQUENCE FROM N.A.
RX   MEDLINE=21876906; PubMed=11882478;
RA   Trudeau V.L., Chiu S., Kennedy S.W., Brooks R.J.;
RT   "Octylphenol (OP) alters the expression of members of the amyloid
RT   protein family in the hypothalamus of the snapping turtle, Chelydra
RT   serpentina serpentina.";
RL   Environ. Health Perspect. 110:269-275(2002).
DR   EMBL; AF541917; AAN04908.1; -.
DR   InterPro; IPR001868; A4_APP.
DR   InterPro; IPR001255; Beta-APP.
DR   Pfam; PF03494; Beta-APP; 1.
DR   PRINTS; PR00203; AMYLOIDA4.
DR   PROSITE; PS00320; A4_INTRA; 1.
FT   NON_TER       1      1
SQ   SEQUENCE   113 AA;  12750 MW;  72515C930496E053 CRC64;

  Query Match             100.0%;  Score 40;  DB 13;  Length 113;
  Best Local Similarity   100.0%;  Pred. No. 0.44;
  Matches    8;  Conservative    0;  Mismatches    0;  Indels    0;  Gaps    0;

Qy          1 EVKMDAEF 8
              ||||||||
Db         11 EVKMDAEF 18


RESULT 7
Q8BPV5
ID   Q8BPV5      PRELIMINARY;      PRT;   218 AA.
AC   Q8BPV5;
DT   01-MAR-2003 (TrEMBLrel. 23, Created)
DT   01-MAR-2003 (TrEMBLrel. 23, Last sequence update)
DT   01-MAR-2003 (TrEMBLrel. 23, Last annotation update)
DE   Amyloid beta (Fragment).
OS   Mus musculus (Mouse).
OC   Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
OC   Mammalia; Eutheria; Rodentia; Sciurognathi; Muridae; Murinae; Mus.
OX   NCBI_TaxID=10090;
RN   [1]
RP   SEQUENCE FROM N.A.
RC   STRAIN=C57BL/6J; TISSUE=Lung;
RX   MEDLINE=22354683; PubMed=12466851;
RA   The FANTOM Consortium,
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RA   the RIKEN Genome Exploration Research Group Phase I & II Team;
RT   "Analysis of the mouse transcriptome based on functional annotation of
RT   60,770 full-length cDNAs.";
RL   Nature 420:563-573(2002).
DR   EMBL; AK052448; BAC34997.1; -.
FT   NON_TER       1      1
SQ   SEQUENCE   218 AA;  24118 MW;  95B55AFDAE1D0EF5 CRC64;

  Query Match             100.0%;  Score 40;  DB 11;  Length 218;
  Best Local Similarity   100.0%;  Pred. No. 0.86;
  Matches    8;  Conservative    0;  Mismatches    0;  Indels    0;  Gaps    0;

Qy          1 EVKMDAEF 8
              ||||||||
Db        116 EVKMDAEF 123


RESULT 8
Q8BPC7
ID   Q8BPC7      PRELIMINARY;      PRT;   384 AA.
AC   Q8BPC7;
DT   01-MAR-2003 (TrEMBLrel. 23, Created)
DT   01-MAR-2003 (TrEMBLrel. 23, Last sequence update)
DT   01-MAR-2003 (TrEMBLrel. 23, Last annotation update)
DE   Amyloid beta (Fragment).
OS   Mus musculus (Mouse).
OC   Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
OC   Mammalia; Eutheria; Rodentia; Sciurognathi; Muridae; Murinae; Mus.
OX   NCBI_TaxID=10090;
RN   [1]
RP   SEQUENCE FROM N.A.
RC   STRAIN=C57BL/6J; TISSUE=Head;
RX   MEDLINE=22354683; PubMed=12466851;
RA   The FANTOM Consortium,
RA   the RIKEN Genome Exploration Research Group Phase I & II Team;
RT   "Analysis of the mouse transcriptome based on functional annotation of
RT   60,770 full-length cDNAs.";
RL   Nature 420:563-573(2002).
DR   EMBL; AK076506; BAC36369.1; -.
FT   NON_TER       1      1
SQ   SEQUENCE   384 AA;  43990 MW;  A81B1AD8AE683173 CRC64;

  Query Match             100.0%;  Score 40;  DB 11;  Length 384;
  Best Local Similarity   100.0%;  Pred. No. 1.5;
  Matches    8;  Conservative    0;  Mismatches    0;  Indels    0;  Gaps    0;

Qy          1 EVKMDAEF 8
              ||||||||
Db        282 EVKMDAEF 289


RESULT 9
O93296
ID   O93296      PRELIMINARY;      PRT;   534 AA.
AC   O93296;
DT   01-NOV-1998 (TrEMBLrel. 08, Created)
DT   01-NOV-1998 (TrEMBLrel. 08, Last sequence update)
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DT   01-OCT-2002 (TrEMBLrel. 22, Last annotation update)
DE   Amyloid protein (Fragment).
OS   Gallus gallus (Chicken).
OC   Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
OC   Archosauria; Aves; Neognathae; Galliformes; Phasianidae; Phasianinae;
OC   Gallus.
OX   NCBI_TaxID=9031;
RN   [1]
RP   SEQUENCE FROM N.A.
RX   MEDLINE=98337885; PubMed=9671674;
RA   Barnes N.Y., Li L., Yoshikawa K., Schwartz L.M., Oppenheim R.W.,
RA   Milligan C.E.;
RT   "Increased production of amyloid precursor protein provides a
RT   substrate for caspase-3 in dying motoneurons.";
RL   J. Neurosci. 18:5869-5880(1998).
DR   EMBL; AF042098; AAC25052.1; -.
DR   HSSP; P05067; 1BA4.
DR   InterPro; IPR001868; A4_APP.
DR   InterPro; IPR001255; Beta-APP.
DR   Pfam; PF02177; A4_EXTRA; 1.
DR   Pfam; PF03494; Beta-APP; 1.
DR   PRINTS; PR00203; AMYLOIDA4.
DR   PROSITE; PS00319; A4_EXTRA; 1.
DR   PROSITE; PS00320; A4_INTRA; 1.
FT   NON_TER       1      1
SQ   SEQUENCE   534 AA;  60597 MW;  FB53ECC2E66D4C92 CRC64;

  Query Match             100.0%;  Score 40;  DB 13;  Length 534;
  Best Local Similarity   100.0%;  Pred. No. 2.1;
  Matches    8;  Conservative    0;  Mismatches    0;  Indels    0;  Gaps    0;

Qy          1 EVKMDAEF 8
              ||||||||
Db        432 EVKMDAEF 439


RESULT 10
Q9PVL1
ID   Q9PVL1      PRELIMINARY;      PRT;   569 AA.
AC   Q9PVL1;
DT   01-MAY-2000 (TrEMBLrel. 13, Created)
DT   01-MAY-2000 (TrEMBLrel. 13, Last sequence update)
DT   01-MAR-2003 (TrEMBLrel. 23, Last annotation update)
DE   Amyloid protein (Fragment).
GN   APP.
OS   Gallus gallus (Chicken).
OC   Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
OC   Archosauria; Aves; Neognathae; Galliformes; Phasianidae; Phasianinae;
OC   Gallus.
OX   NCBI_TaxID=9031;
RN   [1]
RP   SEQUENCE FROM N.A.
RC   TISSUE=Brain;
RA   Coulson E.J., Paliga K., Beyreuther K., Masters C.L.;
RT   "What the evolution of the amyloid protein precursor supergene family
RT   tells us about its function.";
RL   Neurochem. Int. 0:0-0(2000).
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DR   EMBL; AF030341; AAF12698.1; -.
DR   HSSP; P05067; 1BA4.
DR   InterPro; IPR001868; A4_APP.
DR   InterPro; IPR001255; Beta-APP.
DR   Pfam; PF02177; A4_EXTRA; 1.
DR   Pfam; PF03494; Beta-APP; 1.
DR   PRINTS; PR00203; AMYLOIDA4.
DR   PROSITE; PS00319; A4_EXTRA; 1.
DR   PROSITE; PS00320; A4_INTRA; 1.
FT   NON_TER       1      1
SQ   SEQUENCE   569 AA;  64753 MW;  0AB8BB851863A19D CRC64;

  Query Match             100.0%;  Score 40;  DB 13;  Length 569;
  Best Local Similarity   100.0%;  Pred. No. 2.3;
  Matches    8;  Conservative    0;  Mismatches    0;  Indels    0;  Gaps    0;

Qy          1 EVKMDAEF 8
              ||||||||
Db        468 EVKMDAEF 475


RESULT 11
Q99K32
ID   Q99K32      PRELIMINARY;      PRT;   607 AA.
AC   Q99K32;
DT   01-JUN-2001 (TrEMBLrel. 17, Created)
DT   01-JUN-2001 (TrEMBLrel. 17, Last sequence update)
DT   01-OCT-2002 (TrEMBLrel. 22, Last annotation update)
DE   Hypothetical 68.4 kDa protein (Fragment).
GN   APP.
OS   Mus musculus (Mouse).
OC   Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
OC   Mammalia; Eutheria; Rodentia; Sciurognathi; Muridae; Murinae; Mus.
OX   NCBI_TaxID=10090;
RN   [1]
RP   SEQUENCE FROM N.A.
RA   Strausberg R.;
RL   Submitted (MAR-2001) to the EMBL/GenBank/DDBJ databases.
DR   EMBL; BC005490; AAH05490.1; -.
DR   HSSP; P05067; 1AAP.
DR   MGD; MGI:88059; App.
DR   InterPro; IPR001868; A4_APP.
DR   InterPro; IPR001255; Beta-APP.
DR   InterPro; IPR002223; Kunitz_BPTI.
DR   Pfam; PF02177; A4_EXTRA; 1.
DR   Pfam; PF03494; Beta-APP; 1.
DR   Pfam; PF00014; Kunitz_BPTI; 1.
DR   PRINTS; PR00203; AMYLOIDA4.
DR   PRINTS; PR00759; BASICPTASE.
DR   ProDom; PD000222; Kunitz_BPTI; 1.
DR   SMART; SM00131; KU; 1.
DR   PROSITE; PS00319; A4_EXTRA; 1.
DR   PROSITE; PS00320; A4_INTRA; 1.
DR   PROSITE; PS00280; BPTI_KUNITZ_1; 1.
DR   PROSITE; PS50279; BPTI_KUNITZ_2; 1.
KW   Hypothetical protein; Protease inhibitor; Serine protease inhibitor.
FT   NON_TER       1      1
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SQ   SEQUENCE   607 AA;  68391 MW;  BF802214CBA7D172 CRC64;

  Query Match             100.0%;  Score 40;  DB 11;  Length 607;
  Best Local Similarity   100.0%;  Pred. No. 2.4;
  Matches    8;  Conservative    0;  Mismatches    0;  Indels    0;  Gaps    0;

Qy          1 EVKMDAEF 8
              ||||||||
Db        505 EVKMDAEF 512


RESULT 12
Q60496
ID   Q60496      PRELIMINARY;      PRT;   695 AA.
AC   Q60496;
DT   01-NOV-1996 (TrEMBLrel. 01, Created)
DT   01-NOV-1996 (TrEMBLrel. 01, Last sequence update)
DT   01-OCT-2002 (TrEMBLrel. 22, Last annotation update)
DE   Putative amyloid precursor protein.
OS   Cavia sp.
OC   Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
OC   Mammalia; Eutheria; Rodentia; Hystricognathi; Caviidae; Cavia.
OX   NCBI_TaxID=10143;
RN   [1]
RP   SEQUENCE FROM N.A.
RC   TISSUE=Brain;
RX   MEDLINE=97236426; PubMed=9116031;
RA   Beck M., Mueller D., Bigl V.;
RT   "Amyloid precursor protein in Guinea pigs - complete cDNA sequence and
RT   alternative splicing.";
RL   Biochim. Biophys. Acta 1351:17-21(1997).
DR   EMBL; X97631; CAA66230.1; -.
DR   HSSP; P05067; 1BA4.
DR   InterPro; IPR001868; A4_APP.
DR   InterPro; IPR001255; Beta-APP.
DR   Pfam; PF02177; A4_EXTRA; 1.
DR   Pfam; PF03494; Beta-APP; 1.
DR   PRINTS; PR00203; AMYLOIDA4.
DR   SMART; SM00006; A4_EXTRA; 1.
DR   PROSITE; PS00319; A4_EXTRA; 1.
DR   PROSITE; PS00320; A4_INTRA; 1.
SQ   SEQUENCE   695 AA;  78701 MW;  5196A0C4017F16AB CRC64;

  Query Match             100.0%;  Score 40;  DB 11;  Length 695;
  Best Local Similarity   100.0%;  Pred. No. 2.8;
  Matches    8;  Conservative    0;  Mismatches    0;  Indels    0;  Gaps    0;

Qy          1 EVKMDAEF 8
              ||||||||
Db        593 EVKMDAEF 600


RESULT 13
P97487
ID   P97487      PRELIMINARY;      PRT;   695 AA.
AC   P97487; P97942;
DT   01-MAY-1997 (TrEMBLrel. 03, Created)
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DT   01-MAY-1997 (TrEMBLrel. 03, Last sequence update)
DT   01-OCT-2002 (TrEMBLrel. 22, Last annotation update)
DE   Hippocampal amyloid protein.
GN   APP.
OS   Mus musculus (Mouse).
OC   Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
OC   Mammalia; Eutheria; Rodentia; Sciurognathi; Muridae; Murinae; Mus.
OX   NCBI_TaxID=10090;
RN   [1]
RP   SEQUENCE FROM N.A.
RC   STRAIN=SAMP8; TISSUE=Hippocampus;
RA   Flood J.F., Kumar V.B., Sasser T., Word I., Morley J.E.;
RL   Submitted (JAN-1997) to the EMBL/GenBank/DDBJ databases.
RN   [2]
RP   SEQUENCE OF 581-662 FROM N.A.
RC   STRAIN=129SV;
RA   Wragg M.A., Busfield F., Duff K., Korenblat K., Capecchi M.,
RA   Loring J.F., Goate A.M.;
RL   Submitted (DEC-1996) to the EMBL/GenBank/DDBJ databases.
DR   EMBL; U84012; AAB41502.1; -.
DR   EMBL; U82624; AAB40919.1; -.
DR   HSSP; P05067; 1MWP.
DR   MGD; MGI:88059; App.
DR   InterPro; IPR001868; A4_APP.
DR   InterPro; IPR001255; Beta-APP.
DR   Pfam; PF02177; A4_EXTRA; 1.
DR   Pfam; PF03494; Beta-APP; 1.
DR   PRINTS; PR00203; AMYLOIDA4.
DR   SMART; SM00006; A4_EXTRA; 1.
DR   PROSITE; PS00319; A4_EXTRA; 1.
DR   PROSITE; PS00320; A4_INTRA; 1.
SQ   SEQUENCE   695 AA;  78414 MW;  9A5FBE2ED261236E CRC64;

  Query Match             100.0%;  Score 40;  DB 11;  Length 695;
  Best Local Similarity   100.0%;  Pred. No. 2.8;
  Matches    8;  Conservative    0;  Mismatches    0;  Indels    0;  Gaps    0;

Qy          1 EVKMDAEF 8
              ||||||||
Db        593 EVKMDAEF 600


RESULT 14
Q9DGJ8
ID   Q9DGJ8      PRELIMINARY;      PRT;   695 AA.
AC   Q9DGJ8;
DT   01-MAR-2001 (TrEMBLrel. 16, Created)
DT   01-MAR-2001 (TrEMBLrel. 16, Last sequence update)
DT   01-OCT-2002 (TrEMBLrel. 22, Last annotation update)
DE   Beta-amyloid precursor protein 695 isoform.
OS   Gallus gallus (Chicken).
OC   Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
OC   Archosauria; Aves; Neognathae; Galliformes; Phasianidae; Phasianinae;
OC   Gallus.
OX   NCBI_TaxID=9031;
RN   [1]
RP   SEQUENCE FROM N.A.
```

```
RA   Sarasa M., Rodolosse A., Sorribas V.;
RT   "Cloning of full-length chicken beta-amyloid precursor protein
RT   isoforms.";
RL   Submitted (JUL-2000) to the EMBL/GenBank/DDBJ databases.
DR   EMBL; AF289218; AAG00593.1; -.
DR   HSSP; P05067; 1BA4.
DR   InterPro; IPR001868; A4_APP.
DR   InterPro; IPR001255; Beta-APP.
DR   Pfam; PF02177; A4_EXTRA; 1.
DR   Pfam; PF03494; Beta-APP; 1.
DR   PRINTS; PR00203; AMYLOIDA4.
DR   SMART; SM00006; A4_EXTRA; 1.
DR   PROSITE; PS00319; A4_EXTRA; 1.
DR   PROSITE; PS00320; A4_INTRA; 1.
SQ   SEQUENCE   695 AA;  78565 MW;  F201ED02AEC86D95 CRC64;

  Query Match             100.0%;  Score 40;  DB 13;  Length 695;
  Best Local Similarity   100.0%;  Pred. No. 2.8;
  Matches    8;  Conservative    0;  Mismatches    0;  Indels    0;  Gaps    0;

Qy          1 EVKMDAEF 8
              ||||||||
Db        593 EVKMDAEF 600


RESULT 15
Q9DGJ7
ID   Q9DGJ7      PRELIMINARY;      PRT;   751 AA.
AC   Q9DGJ7;
DT   01-MAR-2001 (TrEMBLrel. 16, Created)
DT   01-MAR-2001 (TrEMBLrel. 16, Last sequence update)
DT   01-OCT-2002 (TrEMBLrel. 22, Last annotation update)
DE   Beta-amyloid precursor protein 751 isoform.
OS   Gallus gallus (Chicken).
OC   Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
OC   Archosauria; Aves; Neognathae; Galliformes; Phasianidae; Phasianinae;
OC   Gallus.
OX   NCBI_TaxID=9031;
RN   [1]
RP   SEQUENCE FROM N.A.
RA   Sarasa M., Rodolosse A., Sorribas V.;
RT   "Cloning of full-length chicken beta-amyloid precursor protein
RT   isoforms.";
RL   Submitted (JUL-2000) to the EMBL/GenBank/DDBJ databases.
DR   EMBL; AF289219; AAG00594.1; -.
DR   HSSP; P05067; 1BA4.
DR   InterPro; IPR001868; A4_APP.
DR   InterPro; IPR001255; Beta-APP.
DR   InterPro; IPR002223; Kunitz_BPTI.
DR   Pfam; PF02177; A4_EXTRA; 1.
DR   Pfam; PF03494; Beta-APP; 1.
DR   Pfam; PF00014; Kunitz_BPTI; 1.
DR   PRINTS; PR00203; AMYLOIDA4.
DR   PRINTS; PR00759; BASICPTASE.
DR   ProDom; PD000222; Kunitz_BPTI; 1.
DR   SMART; SM00006; A4_EXTRA; 1.
DR   SMART; SM00131; KU; 1.
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DR   PROSITE; PS00319; A4_EXTRA; 1.
DR   PROSITE; PS00320; A4_INTRA; 1.
DR   PROSITE; PS00280; BPTI_KUNITZ_1; 1.
DR   PROSITE; PS50279; BPTI_KUNITZ_2; 1.
KW   Protease inhibitor; Serine protease inhibitor.
SQ   SEQUENCE   751 AA;  84705 MW;  E78E9413A8033D84 CRC64;

  Query Match             100.0%;  Score 40;  DB 13;  Length 751;
  Best Local Similarity   100.0%;  Pred. No. 3;
  Matches    8;  Conservative    0;  Mismatches    0;  Indels    0;  Gaps    0;

Qy          1 EVKMDAEF 8
              ||||||||
Db        649 EVKMDAEF 656


Search completed: January 21, 2004, 09:25:11
Job time : 2.65201 secs
```

GenCore version 5.1.6

OM protein - protein search, using sw model

Run on: January 21, 2004, 09:15:44 ; Search time 0.397706 Seconds
(without alignments)
945.960 Million cell updates/sec

Title: US-09-869-414A-67
Perfect score: 40
Sequence: 1 EVKMDAEF 8

Scoring table: BLOSUM62
Gapop 10.0 , Gapext 0.5

Searched: 127863 seqs, 47026705 residues

Total number of hits satisfying chosen parameters: 127863

Minimum DB seq length: 0
Maximum DB seq length: 2000000000

Post-processing: Minimum Match 0%
Maximum Match 100%
Listing first 45 summaries

Database : SwissProt_41:*

Pred. No. is the number of results predicted by chance to have a score greater than or equal to the score of the result being printed, and is derived by analysis of the total score distribution.

SUMMARIES

Result No.	Score	% Query Match	Length	DB	ID	Description
1	40	100.0	57	1	A4_URSMA	Q29149 ursus marit
2	40	100.0	58	1	A4_CANFA	Q28280 canis famil
3	40	100.0	58	1	A4_RABIT	Q28748 oryctolagus
4	40	100.0	58	1	A4_SHEEP	Q28757 ovis aries
5	40	100.0	59	1	A4_BOVIN	Q28053 bos taurus
6	40	100.0	751	1	A4_SAISC	Q95241 s amyloid b
7	40	100.0	770	1	A4_CAVPO	Q60495 c amyloid b
8	40	100.0	770	1	A4_HUMAN	P05067 h amyloid b
9	40	100.0	770	1	A4_MACFA	P53601 m amyloid b
10	40	100.0	770	1	A4_MOUSE	P12023 m amyloid b
11	40	100.0	770	1	A4_PIG	P79307 s amyloid b
12	40	100.0	770	1	A4_RAT	P08592 r amyloid b
13	32	80.0	354	1	BCPA_CHLLT	Q46135 chlorobium
14	32	80.0	365	1	BCPA_CHLTE	Q46393 chlorobium
15	32	80.0	1906	1	YFA0_ANASP	Q8ym40 anabaena sp
16	31	77.5	3562	1	PGCV_CHICK	Q90953 gallus gall
17	30	75.0	81	1	RS16_CLOPE	Q8xjp4 clostridium

18	29	72.5	84	1	U222_CAEEL	Q9xvz8	caenorhabdi
19	29	72.5	400	1	YF74_ARCFU	O28698	archaeoglob
20	29	72.5	452	1	F26_YEAST	P32604	saccharomyc
21	29	72.5	463	1	YDI4_SCHPO	Q92342	schizosacch
22	29	72.5	464	1	SPN5_SCHPO	P48010	schizosacch
23	29	72.5	491	1	RNG_HAEIN	P45175	haemophilus
24	29	72.5	526	1	SECD_HELPJ	Q9zj66	helicobacte
25	29	72.5	656	1	V091_FOWPV	O72896	fowlpox vir
26	29	72.5	871	1	POB1_SCHPO	O74653	schizosacch
27	29	72.5	949	1	PODK_MESCR	Q42910	mesembryant
28	29	72.5	4563	1	APB_HUMAN	P04114	homo sapien
29	28	70.0	197	1	OM26_HAEIN	Q57483	haemophilus
30	28	70.0	221	1	PBPH_CAEEL	O16264	caenorhabdi
31	28	70.0	227	1	FA3C_HUMAN	Q92520	homo sapien
32	28	70.0	227	1	FA3C_MOUSE	Q91vu0	mus musculu
33	28	70.0	231	1	RNH_STRCO	Q9x7r6	streptomyce
34	28	70.0	261	1	YN10_ARCFU	O27974	archaeoglob
35	28	70.0	269	1	T2S1_STRFI	O52512	streptomyce
36	28	70.0	299	1	YJ52_STRCO	Q9z513	streptomyce
37	28	70.0	304	1	PH85_KLULA	Q92241	kluyveromyc
38	28	70.0	305	1	PH85_YEAST	P17157	saccharomyc
39	28	70.0	424	1	EF1A_THEAC	P19486	thermoplasm
40	28	70.0	424	1	EF1A_THEVO	Q979t1	thermoplasm
41	28	70.0	673	1	FXO3_HUMAN	O43524	homo sapien
42	28	70.0	695	1	PARE_CAUCR	O54479	caulobacter
43	28	70.0	863	1	PHSG_MYCTU	Q10639	mycobacteri
44	28	70.0	927	1	CC15_SCHPO	Q09822	schizosacch
45	28	70.0	1017	1	MCM6_YEAST	P53091	saccharomyc

ALIGNMENTS

```
RESULT 1
A4_URSMA
ID   A4_URSMA       STANDARD;      PRT;    57 AA.
AC   Q29149;
DT   01-NOV-1997 (Rel. 35, Created)
DT   01-NOV-1997 (Rel. 35, Last sequence update)
DT   30-MAY-2000 (Rel. 39, Last annotation update)
DE   Alzheimer's disease amyloid A4 protein homolog [Contains: Beta-amyloid
DE   protein (Beta-APP) (A-beta)] (Fragment).
GN   APP.
OS   Ursus maritimus (Polar bear) (Thalarctos maritimus).
OC   Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
OC   Mammalia; Eutheria; Carnivora; Fissipedia; Ursidae; Ursus.
OX   NCBI_TaxID=29073;
RN   [1]
RP   SEQUENCE FROM N.A.
RC   TISSUE=Brain;
RX   MEDLINE=92017079; PubMed=1656157;
RA   Johnstone E.M., Chaney M.O., Norris F.H., Pascual R., Little S.P.;
RT   "Conservation of the sequence of the Alzheimer's disease amyloid
RT   peptide in dog, polar bear and five other mammals by cross-species
RT   polymerase chain reaction analysis.";
RL   Brain Res. Mol. Brain Res. 10:299-305(1991).
CC   -!- FUNCTION: FUNCTIONAL NEURONAL RECEPTOR WHICH COUPLES TO
```

```
CC       INTRACELLULAR SIGNALING PATHWAY THROUGH THE GTP-BINDING PROTEIN
CC       G(O) (BY SIMILARITY).
CC   -!- SUBCELLULAR LOCATION: Type I membrane protein.
CC   -!- SIMILARITY: BELONGS TO THE APP FAMILY.
CC   ----------------------------------------------------------------------
CC   This SWISS-PROT entry is copyright. It is produced through a collaboration
CC   between the Swiss Institute of Bioinformatics and the EMBL outstation -
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CC   use by non-profit institutions as long as its content is in no way
CC   modified and this statement is not removed. Usage by and for commercial
CC   entities requires a license agreement (See http://www.isb-sib.ch/announce/
CC   or send an email to license@isb-sib.ch).
CC   ----------------------------------------------------------------------
DR   EMBL; X56128; CAA39593.1; -.
DR   PIR; B60045; B60045.
DR   HSSP; P05067; 1BA4.
DR   InterPro; IPR001868; A4_APP.
DR   InterPro; IPR001255; Beta-APP.
DR   Pfam; PF03494; Beta-APP; 1.
DR   PROSITE; PS00319; A4_EXTRA; PARTIAL.
DR   PROSITE; PS00320; A4_INTRA; PARTIAL.
KW   Glycoprotein; Amyloid; Neurone; Transmembrane.
FT   NON_TER       1      1
FT   CHAIN         6     48       BETA-AMYLOID PROTEIN (POTENTIAL).
FT   DOMAIN       <1     33       EXTRACELLULAR (POTENTIAL).
FT   TRANSMEM     34     57       POTENTIAL.
FT   NON_TER      57     57
SQ   SEQUENCE   57 AA;  6172 MW;  84209D88EBA82DFA CRC64;

  Query Match             100.0%;  Score 40;  DB 1;  Length 57;
  Best Local Similarity   100.0%;  Pred. No. 0.048;
  Matches    8;  Conservative    0;  Mismatches    0;  Indels    0;  Gaps    0;

Qy          1 EVKMDAEF 8
              ||||||||
Db          2 EVKMDAEF 9


RESULT 2
A4_CANFA
ID   A4_CANFA       STANDARD;      PRT;    58 AA.
AC   Q28280;
DT   01-NOV-1997 (Rel. 35, Created)
DT   01-NOV-1997 (Rel. 35, Last sequence update)
DT   30-MAY-2000 (Rel. 39, Last annotation update)
DE   Alzheimer's disease amyloid A4 protein homolog [Contains: Beta-amyloid
DE   protein (Beta-APP) (A-beta)] (Fragment).
GN   APP.
OS   Canis familiaris (Dog).
OC   Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
OC   Mammalia; Eutheria; Carnivora; Fissipedia; Canidae; Canis.
OX   NCBI_TaxID=9615;
RN   [1]
RP   SEQUENCE FROM N.A.
RC   TISSUE=Kidney;
RX   MEDLINE=92017079; PubMed=1656157;
RA   Johnstone E.M., Chaney M.O., Norris F.H., Pascual R., Little S.P.;
```

```
RT   "Conservation of the sequence of the Alzheimer's disease amyloid
RT   peptide in dog, polar bear and five other mammals by cross-species
RT   polymerase chain reaction analysis.";
RL   Brain Res. Mol. Brain Res. 10:299-305(1991).
CC   -!- FUNCTION: FUNCTIONAL NEURONAL RECEPTOR WHICH COUPLES TO
CC       INTRACELLULAR SIGNALING PATHWAY THROUGH THE GTP-BINDING PROTEIN
CC       G(O) (BY SIMILARITY).
CC   -!- SUBCELLULAR LOCATION: Type I membrane protein.
CC   -!- SIMILARITY: BELONGS TO THE APP FAMILY.
CC   ----------------------------------------------------------------------
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CC   entities requires a license agreement (See http://www.isb-sib.ch/announce/
CC   or send an email to license@isb-sib.ch).
CC   ----------------------------------------------------------------------
DR   EMBL; X56125; CAA39590.1; -.
DR   HSSP; P05067; 1BA4.
DR   InterPro; IPR001868; A4_APP.
DR   InterPro; IPR001255; Beta-APP.
DR   Pfam; PF03494; Beta-APP; 1.
DR   PROSITE; PS00319; A4_EXTRA; PARTIAL.
DR   PROSITE; PS00320; A4_INTRA; PARTIAL.
KW   Glycoprotein; Amyloid; Neurone; Transmembrane.
FT   NON_TER       1      1
FT   CHAIN         7     49       BETA-AMYLOID PROTEIN (POTENTIAL).
FT   DOMAIN       <1     34       EXTRACELLULAR (POTENTIAL).
FT   TRANSMEM     35     58       POTENTIAL.
FT   NON_TER      58     58
SQ   SEQUENCE   58 AA;  6285 MW;  8469D488A2E12DFA CRC64;

  Query Match             100.0%;  Score 40;  DB 1;  Length 58;
  Best Local Similarity   100.0%;  Pred. No. 0.049;
  Matches    8;  Conservative    0;  Mismatches    0;  Indels    0;  Gaps    0;

Qy          1 EVKMDAEF 8
              ||||||||
Db          3 EVKMDAEF 10


RESULT 3
A4_RABIT
ID   A4_RABIT       STANDARD;      PRT;    58 AA.
AC   Q28748;
DT   01-NOV-1997 (Rel. 35, Created)
DT   01-NOV-1997 (Rel. 35, Last sequence update)
DT   16-OCT-2001 (Rel. 40, Last annotation update)
DE   Alzheimer's disease amyloid A4 protein homolog [Contains: Beta-amyloid
DE   protein (Beta-APP) (A-beta)] (Fragment).
GN   APP.
OS   Oryctolagus cuniculus (Rabbit).
OC   Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
OC   Mammalia; Eutheria; Lagomorpha; Leporidae; Oryctolagus.
OX   NCBI_TaxID=9986;
RN   [1]
```

```
RP   SEQUENCE FROM N.A.
RC   TISSUE=Brain;
RX   MEDLINE=92017079; PubMed=1656157;
RA   Johnstone E.M., Chaney M.O., Norris F.H., Pascual R., Little S.P.;
RT   "Conservation of the sequence of the Alzheimer's disease amyloid
RT   peptide in dog, polar bear and five other mammals by cross-species
RT   polymerase chain reaction analysis.";
RL   Brain Res. Mol. Brain Res. 10:299-305(1991).
CC   -!- FUNCTION: FUNCTIONAL NEURONAL RECEPTOR WHICH COUPLES TO
CC       INTRACELLULAR SIGNALING PATHWAY THROUGH THE GTP-BINDING PROTEIN
CC       G(O) (BY SIMILARITY).
CC   -!- SUBCELLULAR LOCATION: Type I membrane protein.
CC   -!- SIMILARITY: BELONGS TO THE APP FAMILY.
CC   ----------------------------------------------------------------------
CC   This SWISS-PROT entry is copyright. It is produced through a collaboration
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CC   or send an email to license@isb-sib.ch).
CC   ----------------------------------------------------------------------
DR   EMBL; X56129; CAA39594.1; -.
DR   HSSP; P05067; 1BA4.
DR   InterPro; IPR001868; A4_APP.
DR   InterPro; IPR001255; Beta-APP.
DR   Pfam; PF03494; Beta-APP; 1.
DR   PROSITE; PS00319; A4_EXTRA; PARTIAL.
DR   PROSITE; PS00320; A4_INTRA; PARTIAL.
KW   Glycoprotein; Amyloid; Neurone; Transmembrane.
FT   NON_TER       1      1
FT   CHAIN         6     48       BETA-AMYLOID PROTEIN (POTENTIAL).
FT   DOMAIN       <1     33       EXTRACELLULAR (POTENTIAL).
FT   TRANSMEM     34     57       POTENTIAL.
FT   DOMAIN       58    >58       CYTOPLASMIC (POTENTIAL).
FT   NON_TER      58     58
SQ   SEQUENCE   58 AA;  6300 MW;  F434209D88EBA82D CRC64;

  Query Match             100.0%;  Score 40;  DB 1;  Length 58;
  Best Local Similarity   100.0%;  Pred. No. 0.049;
  Matches    8;  Conservative    0;  Mismatches    0;  Indels    0;  Gaps    0;

Qy          1 EVKMDAEF 8
              ||||||||
Db          2 EVKMDAEF 9


RESULT 4
A4_SHEEP
ID   A4_SHEEP       STANDARD;      PRT;    58 AA.
AC   Q28757;
DT   01-NOV-1997 (Rel. 35, Created)
DT   01-NOV-1997 (Rel. 35, Last sequence update)
DT   30-MAY-2000 (Rel. 39, Last annotation update)
DE   Alzheimer's disease amyloid A4 protein homolog [Contains: Beta-amyloid
DE   protein (Beta-APP) (A-beta)] (Fragment).
GN   APP.
```

```
OS   Ovis aries (Sheep).
OC   Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
OC   Mammalia; Eutheria; Cetartiodactyla; Ruminantia; Pecora; Bovoidea;
OC   Bovidae; Caprinae; Ovis.
OX   NCBI_TaxID=9940;
RN   [1]
RP   SEQUENCE FROM N.A.
RC   TISSUE=Heart;
RX   MEDLINE=92017079; PubMed=1656157;
RA   Johnstone E.M., Chaney M.O., Norris F.H., Pascual R., Little S.P.;
RT   "Conservation of the sequence of the Alzheimer's disease amyloid
RT   peptide in dog, polar bear and five other mammals by cross-species
RT   polymerase chain reaction analysis.";
RL   Brain Res. Mol. Brain Res. 10:299-305(1991).
CC   -!- FUNCTION: FUNCTIONAL NEURONAL RECEPTOR WHICH COUPLES TO
CC       INTRACELLULAR SIGNALING PATHWAY THROUGH THE GTP-BINDING PROTEIN
CC       G(O) (BY SIMILARITY).
CC   -!- SUBCELLULAR LOCATION: Type I membrane protein.
CC   -!- SIMILARITY: BELONGS TO THE APP FAMILY.
CC   ----------------------------------------------------------------------
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CC   or send an email to license@isb-sib.ch).
CC   ----------------------------------------------------------------------
DR   EMBL; X56130; CAA39595.1; -.
DR   HSSP; P05067; 1BA4.
DR   InterPro; IPR001868; A4_APP.
DR   InterPro; IPR001255; Beta-APP.
DR   Pfam; PF03494; Beta-APP; 1.
DR   PROSITE; PS00319; A4_EXTRA; PARTIAL.
DR   PROSITE; PS00320; A4_INTRA; PARTIAL.
KW   Glycoprotein; Amyloid; Neurone; Transmembrane.
FT   NON_TER       1      1
FT   CHAIN         6     48       BETA-AMYLOID PROTEIN (POTENTIAL).
FT   DOMAIN       <1     33       EXTRACELLULAR (POTENTIAL).
FT   TRANSMEM     34     57       POTENTIAL.
FT   DOMAIN       58    >58       CYTOPLASMIC (POTENTIAL).
FT   NON_TER      58     58
SQ   SEQUENCE   58 AA;  6300 MW;  F434209D88EBA82D CRC64;

  Query Match             100.0%;  Score 40;  DB 1;  Length 58;
  Best Local Similarity   100.0%;  Pred. No. 0.049;
  Matches    8;  Conservative    0;  Mismatches    0;  Indels    0;  Gaps    0;

Qy          1 EVKMDAEF 8
              ||||||||
Db          2 EVKMDAEF 9


RESULT 5
A4_BOVIN
ID   A4_BOVIN       STANDARD;      PRT;    59 AA.
AC   Q28053;
```

```
DT   01-NOV-1997 (Rel. 35, Created)
DT   01-NOV-1997 (Rel. 35, Last sequence update)
DT   30-MAY-2000 (Rel. 39, Last annotation update)
DE   Alzheimer's disease amyloid A4 protein homolog [Contains: Beta-amyloid
DE   protein (Beta-APP) (A-beta)] (Fragment).
GN   APP.
OS   Bos taurus (Bovine).
OC   Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
OC   Mammalia; Eutheria; Cetartiodactyla; Ruminantia; Pecora; Bovoidea;
OC   Bovidae; Bovinae; Bos.
OX   NCBI_TaxID=9913;
RN   [1]
RP   SEQUENCE FROM N.A.
RC   TISSUE=Brain;
RX   MEDLINE=92017079; PubMed=1656157;
RA   Johnstone E.M., Chaney M.O., Norris F.H., Pascual R., Little S.P.;
RT   "Conservation of the sequence of the Alzheimer's disease amyloid
RT   peptide in dog, polar bear and five other mammals by cross-species
RT   polymerase chain reaction analysis.";
RL   Brain Res. Mol. Brain Res. 10:299-305(1991).
CC   -!- FUNCTION: FUNCTIONAL NEURONAL RECEPTOR WHICH COUPLES TO
CC       INTRACELLULAR SIGNALING PATHWAY THROUGH THE GTP-BINDING PROTEIN
CC       G(O) (BY SIMILARITY).
CC   -!- SUBCELLULAR LOCATION: Type I membrane protein.
CC   -!- SIMILARITY: BELONGS TO THE APP FAMILY.
CC   ----------------------------------------------------------------------
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CC   entities requires a license agreement (See http://www.isb-sib.ch/announce/
CC   or send an email to license@isb-sib.ch).
CC   ----------------------------------------------------------------------
DR   EMBL; X56124; CAA39589.1; -.
DR   EMBL; X56126; CAA39591.1; -.
DR   HSSP; P05067; 1BA4.
DR   InterPro; IPR001868; A4_APP.
DR   InterPro; IPR001255; Beta-APP.
DR   Pfam; PF03494; Beta-APP; 1.
DR   PROSITE; PS00319; A4_EXTRA; PARTIAL.
DR   PROSITE; PS00320; A4_INTRA; PARTIAL.
KW   Glycoprotein; Amyloid; Neurone; Transmembrane.
FT   NON_TER       1      1
FT   CHAIN         7     49       BETA-AMYLOID PROTEIN (POTENTIAL).
FT   DOMAIN       <1     34       EXTRACELLULAR (POTENTIAL).
FT   TRANSMEM     35     58       POTENTIAL.
FT   DOMAIN       59    >59       CYTOPLASMIC (POTENTIAL).
FT   NON_TER      59     59
SQ   SEQUENCE   59 AA;  6414 MW;  F43469D488A2E12D CRC64;

  Query Match             100.0%;  Score 40;  DB 1;  Length 59;
  Best Local Similarity   100.0%;  Pred. No. 0.05;
  Matches    8;  Conservative    0;  Mismatches    0;  Indels    0;  Gaps    0;

Qy          1 EVKMDAEF 8
              ||||||||
```

```
Db          3 EVKMDAEF 10


RESULT 6
A4_SAISC
ID   A4_SAISC       STANDARD;      PRT;   751 AA.
AC   Q95241;
DT   15-DEC-1998 (Rel. 37, Created)
DT   15-DEC-1998 (Rel. 37, Last sequence update)
DT   15-SEP-2003 (Rel. 42, Last annotation update)
DE   Amyloid beta A4 protein precursor (APP) (Alzheimer's disease amyloid
DE   protein homolog) [Contains: Soluble APP-alpha (S-APP-alpha); Soluble
DE   APP-beta (S-APP-beta); C99; Beta-amyloid protein 42 (Beta-APP42);
DE   Beta-amyloid protein 40 (Beta-APP40); C83; P3(42); P3(40); Gamma-
DE   CTF(59) (Gamma-secretase C-terminal fragment 59); Gamma-CTF(57)
DE   (Gamma-secretase C-terminal fragment 57); Gamma-CTF(50) (Gamma-
DE   secretase C-terminal fragment 50); C31].
GN   APP.
OS   Saimiri sciureus (Common squirrel monkey).
OC   Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
OC   Mammalia; Eutheria; Primates; Platyrrhini; Cebidae; Cebinae; Saimiri.
OX   NCBI_TaxID=9521;
RN   [1]
RP   SEQUENCE FROM N.A.
RC   TISSUE=Kidney, and Liver;
RX   MEDLINE=96108492; PubMed=8532114;
RA   Levy E., Amorim A., Frangione B., Walker L.C.;
RT   "Beta-amyloid precursor protein gene in squirrel monkeys with
RT   cerebral amyloid angiopathy.";
RL   Neurobiol. Aging 16:805-808(1995).
CC   -!- FUNCTION: Functions as a cell surface receptor and performs
CC       physiological functions on the surface of neurons relevant to
CC       neurite growth, neuronal adhesion and axonogenesis. Involved in
CC       cell mobility and transcription regulation through protein-protein
CC       interactions (By similarity). Can promote transcription activation
CC       through binding to APBB1/Tip60 and inhibit Notch signaling through
CC       interaction with Numb (By similarity). Couples to apoptosis-
CC       inducing pathways such as those mediated by G(O) and JIP (By
CC       similarity). Inhibits G(0) alpha ATPase activity (By similarity).
CC       Acts as a kinesin I membrane receptor, mediating the axonal
CC       transport of beta-secretase and presenilin 1 (By similarity). May
CC       be involved in copper homeostasis/oxidative stress through copper
CC       ion reduction. In vitro, copper-metallated APP induces neuronal
CC       death directly or is potentiated through Cu(II)-mediated low-
CC       density lipoprotein oxidation (By similarity). Can regulate
CC       neurite outgrowth through binding to components of the
CC       extracellular matrix such as heparin and collagen I and IV (By
CC       similarity). The splice isoforms that contain the BPTI domain
CC       possess protease inhibitor activity (By similarity).
CC   -!- FUNCTION: Beta-amyloid peptides are lipophilic metal chelators
CC       with metal-reducing activity. Bind transient metals such as
CC       copper, zinc and iron (By similarity).
CC   -!- FUNCTION: The gamma-CTF peptides as well as the caspase-cleaved
CC       peptides, including C31, are potent enhancers of neuronal
CC       apoptosis (By similarity).
CC   -!- SUBUNIT: Binds, via its C-terminal, to the PID domain of several
CC       cytoplasmic proteins, including APBB family members, the APBA
```

```
CC       family, MAPK8IP1, and SHC1, Numb and Dab1 (By similarity). Binding
CC       to Dab1 inhibits its serine phosphorylation (By similarity). Also
CC       interacts with GPCR-like protein BPP, FPRL1, APPBP1, IB1, KNS2
CC       (via its TPR domains) (By similarity), APPBP2 (via BaSS) and DDB1.
CC       In vitro, it binds MAPT via the MT-binding domains (By
CC       similarity). Associates with microtubules in the presence of ATP
CC       and in a kinesin-dependent manner (By similarity).
CC   -!- SUBCELLULAR LOCATION: Type I membrane protein. Cell surface
CC       protein that rapidly becomes internalized via clatherin-coated
CC       pits. During maturation, the immature APP (N-glycosylated in the
CC       endoplasmic reticulum) moves to the Golgi complex where complete
CC       maturation occurs (O-glycosylated and sulfated). After alpha-
CC       secretase cleavage, soluble APP is released into the extracellular
CC       space and the C-terminal is internalized to endosomes and
CC       lysosomes. Some APP accumulates in secretory transport vesicles
CC       leaving the late Golgi compartment and returns to the cell
CC       surface. GammaCTF(59) peptide is located to both the cytoplasm and
CC       nuclei of neurons (By similarity).
CC   -!- ALTERNATIVE PRODUCTS:
CC       Event=Alternative splicing; Named isoforms=2;
CC         Comment=Additional isoforms seem to exist;
CC       Name=APP770;
CC         IsoId=Q95241-1; Sequence=Displayed;
CC       Name=APP695;
CC         IsoId=Q95241-2; Sequence=Not described;
CC   -!- DOMAIN: The basolateral sorting signal (BaSS) is required for
CC       sorting of membrane proteins to the basolateral surface of
CC       epithelial cells (By similarity).
CC   -!- DOMAIN: The NPXY sequence motif found in many tyrosine-
CC       phosphorylated proteins is required for the specific binding of
CC       the PID domain. However additional amino acids either N- or C-
CC       terminal to the NPXY motif are often required for complete
CC       interaction. The PID domain-containing proteins which bind APP
CC       require the YENPTY motif for full interaction. These interactions
CC       are independent of phosphorylation on the terminal tyrosine
CC       residue. The NPXY site is also involved in clatherin-mediated
CC       endocytosis (By similarity).
CC   -!- PTM: Proteolytically processed under normal cellular conditions.
CC       Cleavage by alpha-secretase or alternatively by beta-secretase
CC       leads to generation and extracellular release of soluble APP
CC       peptides, S-APP-alpha and S-APP-beta, respectively, and the
CC       retention of corresponding membrane-anchored C-terminal fragments,
CC       C83 and C99. Subsequent processing of C83 by gamma-secretase
CC       yields P3 peptides. This is the major secretory pathway and is
CC       nonamyloidogenic. Alternatively, presenilin/nicastrin-mediated
CC       gamma-secretase processing of C99 releases the amyloid beta
CC       proteins, amyloid-beta 40 (Abeta40) and amyloid-beta 42 (Abeta42),
CC       major components of amyloid plaques, and the cytotoxic C-terminal
CC       fragments, gammaCTF(50), gammaCTF(57) and gammaCTF(59) (By
CC       similarity).
CC   -!- PTM: Proteolytically cleaved by caspases during neuronal apoptosis
CC       (By similarity). Cleavage at Asp-720 by either caspase-3, -8 or -9
CC       results in the production of the neurotoxic C31 peptide and the
CC       increased production of beta-amyloid peptides (By similarity).
CC   -!- PTM: N- and O-linked glycosylated (By similarity).
CC   -!- PTM: Phosphorylation in the C-terminal on tyrosine, threonine and
CC       serine residues is neuron-specific. Phosphorylation can affect APP
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CC       processing, neuronal differentiation and interaction with other
CC       proteins (By similarity).
CC   -!- MISCELLANEOUS: Chelation of metal ions, notably copper, iron and
CC       zinc, can induce histidine-bridging between beta-amyloid molecules
CC       resulting in beta-amyloid-metal aggregates (By similarity).
CC       Extracellular zinc-binding increases binding of heparin to APP and
CC       inhibits collagen-binding (By similarity).
CC   -!- SIMILARITY: BELONGS TO THE APP FAMILY.
CC   -!- SIMILARITY: Contains 1 BPTI/Kunitz inhibitor domain.
CC   ---------------------------------------------------------------------
CC   This SWISS-PROT entry is copyright. It is produced through a collaboration
CC   between the Swiss Institute of Bioinformatics and the EMBL outstation -
CC   the European Bioinformatics Institute. There are no restrictions on its
CC   use by non-profit institutions as long as its content is in no way
CC   modified and this statement is not removed. Usage by and for commercial
CC   entities requires a license agreement (See http://www.isb-sib.ch/announce/
CC   or send an email to license@isb-sib.ch).
CC   ---------------------------------------------------------------------
DR   EMBL; S81024; AAD14347.1; -.
DR   HSSP; P05067; 1AAP.
DR   InterPro; IPR001868; A4_APP.
DR   InterPro; IPR001255; Beta-APP.
DR   InterPro; IPR002223; Kunitz_BPTI.
DR   Pfam; PF02177; A4_EXTRA; 1.
DR   Pfam; PF03494; Beta-APP; 1.
DR   Pfam; PF00014; Kunitz_BPTI; 1.
DR   PRINTS; PR00203; AMYLOIDA4.
DR   PRINTS; PR00759; BASICPTASE.
DR   ProDom; PD000222; Kunitz_BPTI; 1.
DR   SMART; SM00006; A4_EXTRA; 1.
DR   SMART; SM00131; KU; 1.
DR   PROSITE; PS00319; A4_EXTRA; 1.
DR   PROSITE; PS00320; A4_INTRA; 1.
DR   PROSITE; PS00280; BPTI_KUNITZ_1; 1.
DR   PROSITE; PS50279; BPTI_KUNITZ_2; 1.
KW   Apoptosis; Endocytosis; Cell adhesion; Serine protease inhibitor;
KW   Coated pits; Neurone; Heparin-binding; Metal-binding; Copper; Iron;
KW   Zinc; Signal; Transmembrane; Glycoprotein; Phosphorylation;
KW   Proteoglycan; Amyloid; Alternative splicing.
FT   SIGNAL        1     17       BY SIMILARITY.
FT   CHAIN        18    751       A4 PROTEIN.
FT   CHAIN        18    668       SOLUBLE APP-ALPHA (POTENTIAL).
FT   CHAIN        18    652       SOLUBLE APP-BETA (POTENTIAL).
FT   CHAIN       653    751       C99 (POTENTIAL).
FT   CHAIN       653    694       BETA-AMYLOID PROTEIN 42 (POTENTIAL).
FT   CHAIN       653    692       BETA-AMYLOID PROTEIN 40 (POTENTIAL).
FT   CHAIN       669    751       C83 (POTENTIAL).
FT   CHAIN       669    694       P3(42) (POTENTIAL).
FT   CHAIN       669    692       P3(40) (POTENTIAL).
FT   CHAIN       693    751       GAMMA-CTF(59) (POTENTIAL).
FT   CHAIN       695    751       GAMMA-CTF(57) (POTENTIAL).
FT   CHAIN       702    751       GAMMA-CTF(50) (POTENTIAL).
FT   CHAIN       721    751       C31 (POTENTIAL).
FT   DOMAIN       18    680       EXTRACELLULAR (POTENTIAL).
FT   TRANSMEM    681    704       POTENTIAL.
FT   DOMAIN      705    751       CYTOPLASMIC (POTENTIAL).
FT   DOMAIN       96    110       HEPARIN-BINDING (BY SIMILARITY).
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FT   DOMAIN       181     188       ZINC-BINDING (BY SIMILARITY).
FT   DOMAIN       291     341       BPTI/KUNITZ INHIBITOR.
FT   DOMAIN       316     344       HEPARIN-BINDING (BY SIMILARITY).
FT   DOMAIN       363     428       HEPARIN-BINDING (BY SIMILARITY).
FT   DOMAIN       504     521       COLLAGEN-BINDING (BY SIMILARITY).
FT   DOMAIN       713     732       INTERACTION WITH G(O)-ALPHA
FT                                  (BY SIMILARITY).
FT   DOMAIN       230     260       ASP/GLU-RICH (ACIDIC).
FT   DOMAIN       274     280       POLY-THR.
FT   SITE         144     144       REQUIRED FOR COPPER(II) REDUCTION
FT                                  (BY SIMILARITY).
FT   ACT_SITE     301     302       REACTIVE BOND.
FT   SITE         652     653       CLEAVAGE (BY BETA-SECRETASE)
FT                                  (BY SIMILARITY).
FT   SITE         653     654       CLEAVAGE (BY CASPASE-6) (BY SIMILARITY).
FT   SITE         668     669       CLEAVAGE (BY ALPHA-SECRETASE)
FT                                  (BY SIMILARITY).
FT   SITE         685     685       INVOLVED IN FREE RADICAL PROPAGATION
FT                                  (BY SIMILARITY).
FT   SITE         687     687       INVOLVED IN OXIDATIVE REACTIONS
FT                                  (BY SIMILARITY).
FT   SITE         692     693       CLEAVAGE (BY GAMMA-SECRETASE; SITE 1)
FT                                  (BY SIMILARITY).
FT   SITE         694     695       CLEAVAGE (BY GAMMA-SECRETASE; SITE 2)
FT                                  (BY SIMILARITY).
FT   SITE         701     702       CLEAVAGE (BY GAMMA-SECRETASE; SITE 3)
FT                                  (BY SIMILARITY).
FT   SITE         705     715       BASOLATERAL SORTING SIGNAL
FT                                  (BY SIMILARITY).
FT   SITE         720     721       CLEAVAGE (BY CASPASES-3,-6,-8 OR -9)
FT                                  (BY SIMILARITY).
FT   SITE         738     741       ENDOCYTOSIS SIGNAL.
FT   SITE         740     743       NPXY MOTIF.
FT   METAL        137     137       COPPER (BY SIMILARITY).

  Query Match             100.0%;  Score 40;  DB 1;  Length 751;
  Best Local Similarity   100.0%;  Pred. No. 0.59;
  Matches    8;  Conservative    0;  Mismatches    0;  Indels    0;  Gaps    0;

Qy          1 EVKMDAEF 8
              ||||||||
Db        649 EVKMDAEF 656


RESULT 7
A4_CAVPO
ID   A4_CAVPO       STANDARD;      PRT;   770 AA.
AC   Q60495; Q60496;
DT   15-SEP-2003 (Rel. 42, Created)
DT   15-SEP-2003 (Rel. 42, Last sequence update)
DT   15-SEP-2003 (Rel. 42, Last annotation update)
DE   Amyloid beta A4 protein precursor (APP) (ABPP) (Alzheimer's disease
DE   amyloid protein homolog) [Contains: Soluble APP-alpha (S-APP-alpha);
DE   Soluble APP-beta (S-APP-beta); CTF-alpha; CTF-beta; Beta-amyloid
DE   protein 42 (Beta-APP42); Beta-amyloid protein 40 (Beta-APP40); P3(42);
DE   P3(40); CTF(59) (Gamma-secretase C-terminal fragment 59); Gamma-
DE   CTF(57) (Gamma-secretase C-terminal fragment 57); C31].
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GN   APP.
OS   Cavia porcellus (Guinea pig).
OC   Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
OC   Mammalia; Eutheria; Rodentia; Hystricognathi; Caviidae; Cavia.
OX   NCBI_TaxID=10141;
RN   [1]
RP   SEQUENCE FROM N.A., AND ALTERNATIVE SPLICING.
RC   TISSUE=Brain, and Liver;
RX   MEDLINE=97236426; PubMed=9116031;
RA   Beck M., Mueller D., Bigl V.;
RT   "Amyloid precursor protein in Guinea pigs - complete cDNA sequence and
RT   alternative splicing.";
RL   Biochim. Biophys. Acta 1351:17-21(1997).
RN   [2]
RP   INTERACTION OF BETA-APP40 WITH APOE.
RX   MEDLINE=98007700; PubMed=9349544;
RA   Martel C.L., Mackic J.B., Matsubara E., Governale S., Miguel C.,
RA   Miao W., McComb J.G., Frangione B., Ghiso J., Zlokovic B.V.;
RT   "Isoform-specific effects of apolipoproteins E2, E3, and E4 on
RT   cerebral capillary sequestration and blood-brain barrier transport of
RT   circulating Alzheimer's amyloid beta.";
RL   J. Neurochem. 69:1995-2004(1997).
RN   [3]
RP   PROCESSING.
RX   MEDLINE=20084499; PubMed=10619481;
RA   Beck M., Brueckner M.K., Holzer M., Kaap S., Pannicke T., Arendt T.,
RA   Bigl V.;
RT   "Guinea-pig primary cell cultures provide a model to study expression
RT   and amyloidogenic processing of endogenous amyloid precursor
RT   protein.";
RL   Neuroscience 95:243-254(2000).
RN   [4]
RP   GAMMA-SECRETASE PROCESSING.
RX   MEDLINE=20576391; PubMed=11035007;
RA   Pinnix I., Musunuru U., Tun H., Sridharan A., Golde T., Eckman C.,
RA   Ziani-Cherif C., Onstead L., Sambamurti K.;
RT   "A novel gamma -secretase assay based on detection of the putative
RT   C-terminal fragment-gamma of amyloid beta protein precursor.";
RL   J. Biol. Chem. 276:481-487(2001).
CC   -!- FUNCTION: Functions as a cell surface receptor and performs
CC   physiological functions on the surface of neurons relevant to
CC   neurite growth, neuronal adhesion and axonogenesis. Involved in
CC   cell mobility and transcription regulation through protein-protein
CC   interactions (By similarity). Can promote transcription activation
CC   through binding to APBB1/Tip60 and inhibit Notch signaling through
CC   interaction with Numb (By similarity). Couples to apoptosis-
CC   inducing pathways such as those mediated by G(O) and JIP (By
CC   similarity). Inhibits G(O) alpha ATPase activity (By similarity).
CC   Acts as a kinesin I membrane receptor, mediating the axonal
CC   transport of beta-secretase and presenilin 1 (By similarity). May
CC   be involved in copper homeostasis/oxidative stress through copper
CC   ion reduction (By similarity). In vitro, copper-metallated APP
CC   induces neuronal death directly or is potentiated through Cu(II)-
CC   mediated low-density lipoprotein oxidation (By similarity). Can
CC   regulate neurite outgrowth through binding to components of the
CC   extracellular matrix such as heparin and collagen I and IV (By
CC   similarity). The splice isoforms that contain the BPTI domain

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CC       possess protease inhibitor activity (By similarity).
CC   -!- FUNCTION: Beta-amyloid peptides are lipophilic metal chelators
CC       with metal-reducing activity. Bind transient metals such as
CC       copper, zinc and iron. Beta-amyloid peptides bind to lipoproteins
CC       and apoliproteins E and J in the CSF and to HDL particles in
CC       plasma, inhibiting metal-catalyzed oxidation of lipoproteins.
CC   -!- FUNCTION: Appicans elicit adhesion of neural cells to the
CC       extracellular matrix and may regulate neurite outgrowth in the
CC       brain (By similarity).
CC   -!- FUNCTION: The gamma-CTF peptides as well as the caspase-cleaved
CC       peptides, including C31, are potent enhancers of neuronal
CC       apoptosis (By similarity).
CC   -!- SUBUNIT: Binds, via its C-terminal, to the PID domain of several
CC       cytoplasmic proteins, including APBB family members, the APBA
CC       family, MAPK8IP1, SHC1 and Numb and Dab1 (By similarity). Also
CC       interacts with GPCR-like protein BPP, FPRL1, APPBP1, IB1, KNS2
CC       (via its TPR domains), APPBP2 (via BaSS) and DDB1 (By similarity).
CC       Associates with microtubules in the presence of ATP and in a
CC       kinesin-dependent manner (By similarity). Soluble Abeta40 binds
CC       all three isoforms of APOE, in vitro and in vivo. When lipidated,
CC       ApoE3 appears to be the preferred amyloid binding isoform, while
CC       the apoE4 isoform-beta-APP40 complex is capable of being
CC       transported across the blood-brain barrier.
CC   -!- SUBCELLULAR LOCATION: Type I membrane protein. Cell surface
CC       protein that rapidly becomes internalized via clathrin-coated pits
CC       (By similarity). During maturation, the immature APP (N-
CC       glycosylated in the endoplasmic reticulum) moves to the Golgi
CC       complex where complete maturation occurs (O-glycosylated and
CC       sulfated) (By similarity). After alpha-secretase cleavage, soluble
CC       APP is released into the extracellular space and the C-terminal is
CC       internalized to endosomes and lysosomes (By similarity). Some APP
CC       accumulates in secretory transport vesicles leaving the late Golgi
CC       compartment and returns to the cell surface (By similarity). APP
CC       sorts to the basolateral surface in epithelial cells (By
CC       similatity).
CC   -!- ALTERNATIVE PRODUCTS:
CC       Event=Alternative splicing; Named isoforms=2;
CC         Comment=Additional isoforms, missing exons 7,8 and 15, seem to
CC         exist. The L-isoforms, missing exon 15, are referred to as
CC         appicans;
CC       Name=APP770;
CC         IsoId=Q60495-1; Sequence=Displayed;
CC       Name=APP695;
CC         IsoId=Q60495-2; Sequence=VSP_007221, VSP_007222;
CC   -!- TISSUE SPECIFICITY: Isoform APP695 is the major isoform found in
CC       brain. The longer isoforms containing the BPTI domain are
CC       predominantly expressed in peripheral organs such as muscle and
CC       liver.
CC   -!- INDUCTION: Increased levels during neuronal differentiation.
CC   -!- DOMAIN: The basolateral sorting signal (BaSS) is required for
CC       sorting of membrane proteins to the basolateral surface of
CC       epithelial cells.
CC   -!- DOMAIN: The NPXY sequence motif found in many tyrosine-
CC       phosphorylated proteins is required for the specific binding of
CC       the PID domain. However additional amino acids either N- or C-
CC       terminal to the NPXY motif are often required for complete
CC       interaction. The PID domain-containing proteins which bind APP
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CC       require the YENPTY motif for full interaction. These interactions
CC       are independent of phosphorylation on the terminal tyrosine
CC       residue (By similarity). The NPXY site is also involved in
CC       clatherin-mediated endocytosis.
CC   -!- PTM: Proteolytically processed under normal cellular conditions.
CC       Cleavage by alpha-secretase or alternatively by beta-secretase
CC       leads to generation and extracellular release of soluble APP
CC       peptides, S-APP-alpha and S-APP-beta, respectively, and the
CC       retention of corresponding membrane-anchored C-terminal fragments,
CC       CTF-alpha and CTF-beta. Subsequent processing of CTF-alpha by
CC       gamma-secretase yields P3 peptides. This is the major secretory
CC       pathway and is nonamyloidogenic. Alternatively,
CC       presenilin/nicastrin-mediated gamma-secretase processing of CTF-
CC       beta releases the amyloid beta proteins, amyloid-beta 40 (Abeta40)
CC       and amyloid-beta 42 (Abeta42), major components of amyloid
CC       plaques, and the corresponding cytotoxic C-terminal fragments
CC       (CTFs).
CC   -!- PTM: Proteolytically cleaved by caspase-3 during neuronal
CC       apoptosis (By similarity).
CC   -!- PTM: N- and O-linked glycosylated. O-linkage of chondroitin
CC       sulfate to the L-APP isoforms produces the APP proteoglycan core
CC       proteins, the appicans (By similarity).
CC   -!- PTM: Phosphorylation in the C-terminal on tyrosine, threonine and
CC       serine residues is neuron-specific (By similarity).
CC       Phosphorylation can affect APP processing, neuronal
CC       differentiation and interaction with other proteins.
CC   -!- PTM: Extracellular binding and reduction of copper, results in a
CC       corresponding oxidation of Cys-144 and Cys-158, and the formation
CC       of a disulfide bond (By similarity).
CC   -!- MISCELLANEOUS: Chelation of metal ions, notably copper, iron and
CC       zinc, can induce histidine-bridging between beta-amyloid molecules
CC       resulting in beta-amyloid-metal aggregates.
CC   -!- SIMILARITY: BELONGS TO THE APP FAMILY.
CC   -!- SIMILARITY: Contains 1 BPTI/Kunitz inhibitor domain.
CC   ---------------------------------------------------------------------
CC   This SWISS-PROT entry is copyright. It is produced through a collaboration
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CC   or send an email to license@isb-sib.ch).
CC   ---------------------------------------------------------------------
DR   EMBL; X97631; CAA66230.1; -.
DR   EMBL; X99198; CAA67589.1; -.
DR   HSSP; P05067; 1BA4.
DR   InterPro; IPR008155; A4_APP.
DR   InterPro; IPR008154; A4_extra.
DR   InterPro; IPR001255; Beta-APP.
DR   Pfam; PF00014; Kunitz_BPTI; 1.
DR   PRINTS; PR00203; AMYLOIDA4.
DR   ProDom; PD000222; Kunitz_BPTI; 1.
DR   SMART; SM00006; A4_EXTRA; 1.
DR   SMART; SM00131; KU; 1.
DR   PROSITE; PS00319; A4_EXTRA; 1.
DR   PROSITE; PS00320; A4_INTRA; 1.
DR   PROSITE; PS00280; BPTI_KUNITZ_1; 1.
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DR   PROSITE; PS50279; BPTI_KUNITZ_2; 1.
KW   Apoptosis; Endocytosis; Cell adhesion; Serine protease inhibitor;
KW   Coated pits; Neurone; Heparin-binding; Metal-binding; Copper; Iron;
KW   Zinc; Signal; Transmembrane; Glycoprotein; Phosphorylation;
KW   Proteoglycan; Alternative splicing; Amyloid.
FT   SIGNAL        1     17       BY SIMILARITY.
FT   CHAIN        18    770       AMYLOID BETA A4 PROTEIN.
FT   CHAIN        18    687       SOLUBLE APP-ALPHA (BY SIMILARITY).
FT   CHAIN        18    671       SOLUBLE APP-BETA (BY SIMILARITY).
FT   CHAIN       672    770       CTF-ALPHA (BY SIMILARITY).
FT   CHAIN       672    713       BETA-AMYLOID PROTEIN 42 (BY SIMILARITY).
FT   CHAIN       672    711       BETA-AMYLOID PROTEIN 40 (BY SIMILARITY).
FT   CHAIN       688    770       CTF-BETA (BY SIMILARITY).
FT   CHAIN       688    713       P3(42) (BY SIMILARITY).
FT   CHAIN       688    711       P3(40) (BY SIMILARITY).
FT   CHAIN       712    770       GAMMA-CTF(59) (BY SIMILARITY).
FT   CHAIN       714    770       GAMMA-CTF(57) (BY SIMILARITY).
FT   CHAIN       740    770       C31 (BY SIMILARITY).

  Query Match             100.0%;  Score 40;  DB 1;  Length 770;
  Best Local Similarity   100.0%;  Pred. No. 0.61;
  Matches    8;  Conservative    0;  Mismatches    0;  Indels    0;  Gaps    0;

Qy          1 EVKMDAEF 8
              ||||||||
Db        668 EVKMDAEF 675


RESULT 8
A4_HUMAN
ID   A4_HUMAN       STANDARD;      PRT;   770 AA.
AC   P05067; P09000; P78438; Q13764; Q13778; Q13793; Q16011; Q9BT38;
AC   Q9UCB6; Q9UQ58;
DT   13-AUG-1987 (Rel. 05, Created)
DT   01-NOV-1991 (Rel. 20, Last sequence update)
DT   15-SEP-2003 (Rel. 42, Last annotation update)
DE   Amyloid beta A4 protein precursor (APP) (ABPP) (Alzheimer's disease
DE   amyloid protein) (Cerebral vascular amyloid peptide) (CVAP) (Protease
DE   nexin-II) (PN-II) (APPI) (PreA4) [Contains: Soluble APP-alpha (S-APP-
DE   alpha); Soluble APP-beta (S-APP-beta); C99; Beta-amyloid protein 42
DE   (Beta-APP42); Beta-amyloid protein 40 (Beta-APP40); C83; P3(42);
DE   P3(40); Gamma-CTF(59) (Gamma-secretase C-terminal fragment 59)
DE   (Amyloid intracellular domain 59) (AID(59)); Gamma-CTF(57) (Gamma-
DE   secretase C-terminal fragment 57) (Amyloid intracellular domain 57)
DE   (AID(57)); Gamma-CTF(50) (Gamma-secretase C-terminal fragment 50)
DE   (Amyloid intracellular domain 50) (AID(50)); C31].
GN   APP OR A4 OR AD1.
OS   Homo sapiens (Human).
OC   Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
OC   Mammalia; Eutheria; Primates; Catarrhini; Hominidae; Homo.
OX   NCBI_TaxID=9606;
RN   [1]
RP   SEQUENCE FROM N.A. (ISOFORM APP695).
RC   TISSUE=Brain;
RX   MEDLINE=87144572; PubMed=2881207;
RA   Kang J., Lemaire H.-G., Unterbeck A., Salbaum J.M., Masters C.L.,
RA   Grzeschik K.-H., Multhaup G., Beyreuther K., Mueller-Hill B.;
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RT "The precursor of Alzheimer's disease amyloid A4 protein resembles a
RT cell-surface receptor.";
RL Nature 325:733-736(1987).
RN [2]
RP SEQUENCE FROM N.A. (ISOFORM APP751).
RC TISSUE=Brain;
RX MEDLINE=88122639; PubMed=2893289;
RA Ponte P., Gonzalez-Dewhitt P., Schilling J., Miller J., Hsu D.,
RA Greenberg B., Davis K., Wallace W., Lieberburg I., Fuller F.,
RA Cordell B.;
RT "A new A4 amyloid mRNA contains a domain homologous to serine
RT proteinase inhibitors.";
RL Nature 331:525-527(1988).
RN [3]
RP SEQUENCE FROM N.A. (ISOFORM APP695).
RX MEDLINE=89128427; PubMed=2783775;
RA Lemaire H.-G., Salbaum J.M., Multhaup G., Kang J., Bayney R.M.,
RA Unterbeck A., Beyreuther K., Mueller-Hill B.;
RT "The PreA4(695) precursor protein of Alzheimer's disease A4 amyloid
RT is encoded by 16 exons.";
RL Nucleic Acids Res. 17:517-522(1989).
RN [4]
RP SEQUENCE FROM N.A. (ISOFORM APP770).
RX MEDLINE=90236318; PubMed=2110105;
RA Yoshikai S.-I., Sasaki H., Doh-Ura K., Furuya H., Sakaki Y.;
RT "Genomic organization of the human amyloid beta-protein precursor
RT gene.";
RL Gene 87:257-263(1990).
RN [5]
RP ERRATUM, AND REVISIONS.
RA Yoshikai S.-I., Sasaki H., Doh-ura K., Furuya H., Sakaki Y.;
RL Gene 102:291-292(1991).
RN [6]
RP SEQUENCE FROM N.A. (ISOFORM L-APP733).
RC TISSUE=Leukocyte;
RX MEDLINE=92268136; PubMed=1587857;
RA Koenig G., Moenning U., Czech C., Prior R., Banati R.,
RA Schreiter-Gasser U., Bauer J., Masters C.L., Beyreuther K.;
RT "Identification and differential expression of a novel alternative
RT splice isoform of the beta A4 amyloid precursor protein (APP) mRNA in
RT leukocytes and brain microglial cells.";
RL J. Biol. Chem. 267:10804-10809(1992).
RN [7]
RP SEQUENCE FROM N.A. (ISOFORM APP770).
RX MEDLINE=97263807; PubMed=9108164;
RA Hattori M., Tsukahara F., Furuhata Y., Tanahashi H., Hirose M.,
RA Saito M., Tsukuni S., Sakaki Y.;
RT "A novel method for making nested deletions and its application for
RT sequencing of a 300 kb region of human APP locus.";
RL Nucleic Acids Res. 25:1802-1808(1997).
RN [8]
RP SEQUENCE FROM N.A. (ISOFORM APP305).
RC TISSUE=Pancreas;
RX MEDLINE=22388257; PubMed=12477932;
RA Strausberg R.L., Feingold E.A., Grouse L.H., Derge J.G.,
RA Klausner R.D., Collins F.S., Wagner L., Shenmen C.M., Schuler G.D.,
RA Altschul S.F., Zeeberg B., Buetow K.H., Schaefer C.F., Bhat N.K.,

RA Hopkins R.F., Jordan H., Moore T., Max S.I., Wang J., Hsieh F.,
RA Diatchenko L., Marusina K., Farmer A.A., Rubin G.M., Hong L.,
RA Stapleton M., Soares M.B., Bonaldo M.F., Casavant T.L., Scheetz T.E.,
RA Brownstein M.J., Usdin T.B., Toshiyuki S., Carninci P., Prange C.,
RA Raha S.S., Loquellano N.A., Peters G.J., Abramson R.D., Mullahy S.J.,
RA Bosak S.A., McEwan P.J., McKernan K.J., Malek J.A., Gunaratne P.H.,
RA Richards S., Worley K.C., Hale S., Garcia A.M., Gay L.J., Hulyk S.W.,
RA Villalon D.K., Muzny D.M., Sodergren E.J., Lu X., Gibbs R.A.,
RA Fahey J., Helton E., Ketteman M., Madan A., Rodrigues S., Sanchez A.,
RA Whiting M., Madan A., Young A.C., Shevchenko Y., Bouffard G.G.,
RA Blakesley R.W., Touchman J.W., Green E.D., Dickson M.C.,
RA Rodriguez A.C., Grimwood J., Schmutz J., Myers R.M.,
RA Butterfield Y.S.N., Krzywinski M.I., Skalska U., Smailus D.E.,
RA Schnerch A., Schein J.E., Jones S.J.M., Marra M.A.;
RT "Generation and initial analysis of more than 15,000 full-length
RT human and mouse cDNA sequences.";
RL Proc. Natl. Acad. Sci. U.S.A. 99:16899-16903(2002).
RN [9]
RP SEQUENCE OF 1-10 FROM N.A.
RC TISSUE=Liver;
RX MEDLINE=89016647; PubMed=3140222;
RA Schon E.A., Mita S., Sadlock J., Herbert J.;
RT "A cDNA specifying the human amyloid beta precursor protein (ABPP)
RT encodes a 95-kDa polypeptide.";
RL Nucleic Acids Res. 16:9351-9351(1988).
RN [10]
RP ERRATUM, AND REVISIONS.
RA Mita S., Sadlock J., Herbert J., Schon E.A.;
RL Nucleic Acids Res. 16:11402-11402(1988).
RN [11]
RP SEQUENCE OF 1-75 FROM N.A.
RX MEDLINE=89165870; PubMed=2538123;
RA La Fauci G., Lahiri D.K., Salton S.R., Robakis N.K.;
RT "Characterization of the 5'-end region and the first two exons of the
RT beta-protein precursor gene.";
RL Biochem. Biophys. Res. Commun. 159:297-304(1989).
RN [12]
RP SEQUENCE OF 18-50.
RC TISSUE=Fibroblast;
RX MEDLINE=87250462; PubMed=3597385;
RA van Nostrand W.E., Cunningham D.D.;
RT "Purification of protease nexin II from human fibroblasts.";
RL J. Biol. Chem. 262:8508-8514(1987).
RN [13]
RP PARTIAL SEQUENCE FROM N.A. (ISOFORM APP751).
RC TISSUE=Brain;
RX MEDLINE=89346754; PubMed=2569763;
RA de Sauvage F., Octave J.N.;
RT "A novel mRNA of the A4 amyloid precursor gene coding for a possibly
RT secreted protein.";
RL Science 245:651-653(1989).
RN [14]
RP PARTIAL SEQUENCE FROM N.A. (ISOFORM APP695).
RC TISSUE=Brain;
RX MEDLINE=87231971; PubMed=3035574;
RA Robakis N.K., Ramakrishna N., Wolfe G., Wisniewski H.M.;
RT "Molecular cloning and characterization of a cDNA encoding the

RT cerebrovascular and the neuritic plaque amyloid peptides.";
RL Proc. Natl. Acad. Sci. U.S.A. 84:4190-4194(1987).
RN [15]
RP SEQUENCE OF 286-366 FROM N.A.
RX MEDLINE=88122640; PubMed=2893290;
RA Tanzi R.E., McClatchey A.I., Lamperti E.D., Villa-Komaroff L.,
RA Gusella J.F., Neve R.L.;
RT "Protease inhibitor domain encoded by an amyloid protein precursor
RT mRNA associated with Alzheimer's disease.";
RL Nature 331:528-530(1988).
RN [16]
RP SEQUENCE OF 287-367 FROM N.A.
RX MEDLINE=88122641; PubMed=2893291;
RA Kitaguchi N., Takahashi Y., Tokushima Y., Shiojiri S., Ito H.;
RT "Novel precursor of Alzheimer's disease amyloid protein shows
RT protease inhibitory activity.";
RL Nature 331:530-532(1988).
RN [17]
RP SEQUENCE OF 507-770 FROM N.A.
RC TISSUE=Brain cortex;
RX MEDLINE=88124954; PubMed=2893379;
RA Zain S.B., Salim M., Chou W.G., Sajdel-Sulkowska E.M., Majocha R.E.,
RA Marotta C.A.;
RT "Molecular cloning of amyloid cDNA derived from mRNA of the Alzheimer
RT disease brain: coding and noncoding regions of the fetal precursor
RT mRNA are expressed in the cortex.";
RL Proc. Natl. Acad. Sci. U.S.A. 85:929-933(1988).
RN [18]
RP SEQUENCE OF 523-555, AND COLLAGEN-BINDING DOMAIN.
RX MEDLINE=96139497; PubMed=8576160;
RA Beher D., Hesse L., Masters C.L., Multhaup G.;
RT "Regulation of amyloid protein precursor (APP) binding to collagen and
RT mapping of the binding sites on APP and collagen type I.";
RL J. Biol. Chem. 271:1613-1620(1996).
RN [19]
RP SEQUENCE OF 656-737 FROM N.A.
RX MEDLINE=89392030; PubMed=2675837;
RA Johnstone E.M., Chaney M.O., Moore R.E., Ward K.E., Norris F.H.,
RA Little S.P.;
RT "Alzheimer's disease amyloid peptide is encoded by two exons and shows
RT similarity to soybean trypsin inhibitor.";
RL Biochem. Biophys. Res. Commun. 163:1248-1255(1989).
RN [20]
RP SEQUENCE OF 672-681.
RC TISSUE=Brain cortex;
RX MEDLINE=88035004; PubMed=3312495;
RA Pardridge W.M., Vinters H.V., Yang J., Eisenberg J., Choi T.B.,
RA Tourtellotte W.W., Huebner V., Shively J.E.;
RT "Amyloid angiopathy of Alzheimer's disease: amino acid composition
RT and partial sequence of a 4,200-dalton peptide isolated from cortical
RT microvessels.";
RL J. Neurochem. 49:1394-1401(1987).
RN [21]
RP SEQUENCE OF 674-770 FROM N.A.
RC TISSUE=Brain;
RX MEDLINE=87120328; PubMed=3810169;
RA Goldgaber D., Lerman M.I., McBride O.W., Saffiotti U., Gajdusek D.C.;

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RT   "Characterization and chromosomal localization of a cDNA encoding
RT   brain amyloid of Alzheimer's disease.";

  Query Match             100.0%;  Score 40;  DB 1;  Length 770;
  Best Local Similarity   100.0%;  Pred. No. 0.61;
  Matches    8;  Conservative    0;  Mismatches    0;  Indels    0;  Gaps    0;

Qy          1 EVKMDAEF 8
              ||||||||
Db        668 EVKMDAEF 675


RESULT 9
A4_MACFA
ID   A4_MACFA       STANDARD;      PRT;   770 AA.
AC   P53601; Q95KN7;
DT   01-OCT-1996 (Rel. 34, Created)
DT   28-FEB-2003 (Rel. 41, Last sequence update)
DT   28-FEB-2003 (Rel. 41, Last annotation update)
DE   Amyloid beta A4 protein precursor (APP) (ABPP) (Alzheimer's disease
DE   amyloid protein homolog) [Contains: Soluble APP-alpha (S-APP-alpha);
DE   Soluble APP-beta (S-APP-beta); C99; Beta-amyloid protein 42 (Beta-
DE   APP42); Beta-amyloid protein 40 (Beta-APP40); C83; P3(42); P3(40);
DE   Gamma-CTF(59) (Gamma-secretase C-terminal fragment 59); Gamma-CTF(57)
DE   (Gamma-secretase C-terminal fragment 57); Gamma-CTF(50) (Gamma-
DE   secretase C-terminal fragment 50); C31].
GN   APP.
OS   Macaca fascicularis (Crab eating macaque) (Cynomolgus monkey).
OC   Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
OC   Mammalia; Eutheria; Primates; Catarrhini; Cercopithecidae;
OC   Cercopithecinae; Macaca.
OX   NCBI_TaxID=9541;
RN   [1]
RP   SEQUENCE FROM N.A. (ISOFORMS APP695 AND APP770).
RC   TISSUE=Cerebellum;
RX   MEDLINE=91273117; PubMed=1905108;
RA   Podlisny M.B., Tolan D.R., Selkoe D.J.;
RT   "Homology of the amyloid beta protein precursor in monkey and human
RT   supports a primate model for beta amyloidosis in Alzheimer's
RT   disease.";
RL   Am. J. Pathol. 138:1423-1435(1991).
CC   -!- FUNCTION: Functions as a cell surface receptor and performs
CC       physiological functions on the surface of neurons relevant to
CC       neurite growth, neuronal adhesion and axonogenesis. Involved in
CC       cell mobility and transcription regulation through protein-protein
CC       interactions (By similarity). Can promote transcription activation
CC       through binding to APBB1/Tip60 and inhibit Notch signaling through
CC       interaction with Numb (By similarity). Couples to apoptosis-
CC       inducing pathways such as those mediated by G(O) and JIP (By
CC       similarity). Inhibits G(0) alpha ATPase activity (By similarity).
CC       Acts as a kinesin I membrane receptor, mediating the axonal
CC       transport of beta-secretase and presenilin 1 (By similarity). May
CC       be involved in copper homeostasis/oxidative stress through copper
CC       ion reduction. In vitro, copper-metallated APP induces neuronal
CC       death directly or is potentiated through Cu(II)-mediated low-
CC       density lipoprotein oxidation (By similarity). Can regulate
CC       neurite outgrowth through binding to components of the
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CC       extracellular matrix such as heparin and collagen I and IV (By
CC       similarity). The splice isoforms that contain the BPTI domain
CC       possess protease inhibitor activity (By similarity).
CC   -!- FUNCTION: Beta-amyloid peptides are lipophilic metal chelators
CC       with metal-reducing activity. Bind transient metals such as
CC       copper, zinc and iron (By similarity).
CC   -!- FUNCTION: The gamma-CTF peptides as well as the caspase-cleaved
CC       peptides, including C31, are potent enhancers of neuronal
CC       apoptosis (By similarity).
CC   -!- SUBUNIT: Binds, via its C-terminal, to the PID domain of several
CC       cytoplasmic proteins, including APBB family members, the APBA
CC       family, MAPK8IP1, and SHC1, Numb and Dab1 (By similarity). Binding
CC       to Dab1 inhibits its serine phosphorylation (By similarity). Also
CC       interacts with GPCR-like protein BPP, FPRL1, APPBP1, IB1, KNS2
CC       (via its TPR domains) (By similarity), APPBP2 (via BaSS) and DDB1.
CC       In vitro, it binds MAPT via the MT-binding domains (By
CC       similarity). Associates with microtubules in the presence of ATP
CC       and in a kinesin-dependent manner (By similarity).
CC   -!- SUBCELLULAR LOCATION: Type I membrane protein. Cell surface
CC       protein that rapidly becomes internalized via clatherin-coated
CC       pits. During maturation, the immature APP (N-glycosylated in the
CC       endoplasmic reticulum) moves to the Golgi complex where complete
CC       maturation occurs (O-glycosylated and sulfated). After alpha-
CC       secretase cleavage, soluble APP is released into the extracellular
CC       space and the C-terminal is internalized to endosomes and
CC       lysosomes. Some APP accumulates in secretory transport vesicles
CC       leaving the late Golgi compartment and returns to the cell
CC       surface. GammaCTF(59) peptide is located to both the cytoplasm and
CC       nuclei of neurons (By similarity).
CC   -!- ALTERNATIVE PRODUCTS:
CC       Event=Alternative splicing; Named isoforms=2;
CC         Comment=Additional isoforms seem to exist;
CC       Name=APP770;
CC         IsoId=P53601-1; Sequence=Displayed;
CC       Name=APP695;
CC         IsoId=P53601-2; Sequence=VSP_000010, VSP_000011;
CC   -!- DOMAIN: The basolateral sorting signal (BaSS) is required for
CC       sorting of membrane proteins to the basolateral surface of
CC       epithelial cells (By similarity).
CC   -!- DOMAIN: The NPXY sequence motif found in many tyrosine-
CC       phosphorylated proteins is required for the specific binding of
CC       the PID domain. However additional amino acids either N- or C-
CC       terminal to the NPXY motif are often required for complete
CC       interaction. The PID domain-containing proteins which bind APP
CC       require the YENPTY motif for full interaction. These interactions
CC       are independent of phosphorylation on the terminal tyrosine
CC       residue. The NPXY site is also involved in clatherin-mediated
CC       endocytosis (By similarity).
CC   -!- PTM: Proteolytically processed under normal cellular conditions.
CC       Cleavage by alpha-secretase or alternatively by beta-secretase
CC       leads to generation and extracellular release of soluble APP
CC       peptides, S-APP-alpha and S-APP-beta, respectively, and the
CC       retention of corresponding membrane-anchored C-terminal fragments,
CC       C83 and C99. Subsequent processing of C83 by gamma-secretase
CC       yields P3 peptides. This is the major secretory pathway and is
CC       nonamyloidogenic. Alternatively, presenilin/nicastrin-mediated
CC       gamma-secretase processing of C99 releases the amyloid beta
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CC       proteins, amyloid-beta 40 (Abeta40) and amyloid-beta 42 (Abeta42),
CC       major components of amyloid plaques, and the cytotoxic C-terminal
CC       fragments, gammaCTF(50), gammaCTF(57) and gammaCTF(59) (By
CC       similarity).
CC   -!- PTM: Proteolytically cleaved by caspases during neuronal apoptosis
CC       (By similarity). Cleavage at Asp-739 by either caspase-3, -8 or -9
CC       results in the production of the neurotoxic C31 peptide and the
CC       increased production of beta-amyloid peptides (By similarity).
CC   -!- PTM: N- and O-linked glycosylated (By similarity).
CC   -!- PTM: Phosphorylation in the C-terminal on tyrosine, threonine and
CC       serine residues is neuron-specific. Phosphorylation can affect APP
CC       processing, neuronal differentiation and interaction with other
CC       proteins (By similarity).
CC   -!- MISCELLANEOUS: Chelation of metal ions, notably copper, iron and
CC       zinc, can induce histidine-bridging between beta-amyloid molecules
CC       resulting in beta-amyloid-metal aggregates (By similarity).
CC       Extracellular zinc-binding increases binding of heparin to APP and
CC       inhibits collagen-binding (By similarity).
CC   -!- SIMILARITY: BELONGS TO THE APP FAMILY.
CC   -!- SIMILARITY: Contains 1 BPTI/Kunitz inhibitor domain.
CC   ----------------------------------------------------------------------
CC   This SWISS-PROT entry is copyright. It is produced through a collaboration
CC   between the Swiss Institute of Bioinformatics and the EMBL outstation -
CC   the European Bioinformatics Institute. There are no restrictions on its
CC   use by non-profit institutions as long as its content is in no way
CC   modified and this statement is not removed. Usage by and for commercial
CC   entities requires a license agreement (See http://www.isb-sib.ch/announce/
CC   or send an email to license@isb-sib.ch).
CC   ----------------------------------------------------------------------
DR   EMBL; M58727; AAA36829.1; -.
DR   EMBL; M58726; AAA36828.1; -.
DR   HSSP; P05067; 1AAP.
DR   InterPro; IPR001868; A4_APP.
DR   InterPro; IPR002223; Kunitz_BPTI.
DR   Pfam; PF02177; A4_EXTRA; 1.
DR   Pfam; PF03494; Beta-APP; 1.
DR   Pfam; PF00014; Kunitz_BPTI; 1.
DR   PRINTS; PR00759; BASICPTASE.
DR   ProDom; PD000222; Kunitz_BPTI; 1.
DR   SMART; SM00006; A4_EXTRA; 1.
DR   SMART; SM00131; KU; 1.
DR   PROSITE; PS00319; A4_EXTRA; 1.
DR   PROSITE; PS00320; A4_INTRA; 1.
DR   PROSITE; PS00280; BPTI_KUNITZ_1; 1.
DR   PROSITE; PS50279; BPTI_KUNITZ_2; 1.
KW   Apoptosis; Endocytosis; Cell adhesion; Serine protease inhibitor;
KW   Coated pits; Neurone; Heparin-binding; Metal-binding; Copper; Iron;
KW   Zinc; Signal; Transmembrane; Glycoprotein; Phosphorylation;
KW   Proteoglycan; Alternative splicing; Amyloid.
FT   SIGNAL        1     17       BY SIMILARITY.
FT   CHAIN        18    770       AMYLOID BETA A4 PROTEIN.
FT   CHAIN        18    687       SOLUBLE APP-ALPHA (POTENTIAL).
FT   CHAIN        18    671       SOLUBLE APP-BETA (POTENTIAL).
FT   CHAIN       672    770       C99 (POTENTIAL).
FT   CHAIN       672    713       BETA-AMYLOID PROTEIN 42 (POTENTIAL).
FT   CHAIN       672    711       BETA-AMYLOID PROTEIN 40 (POTENTIAL).
FT   CHAIN       688    770       C83 (POTENTIAL).
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FT   CHAIN        688    713       P3(42) (POTENTIAL).
FT   CHAIN        688    711       P3(40) (POTENTIAL).
FT   CHAIN        712    770       GAMMA-CTF(59) (POTENTIAL).
FT   CHAIN        714    770       GAMMA-CTF(57) (POTENTIAL).
FT   CHAIN        721    770       GAMMA-CTF(50) (POTENTIAL).
FT   CHAIN        740    770       C31 (POTENTIAL).
FT   DOMAIN        18    699       EXTRACELLULAR (POTENTIAL).
FT   TRANSMEM     700    723       POTENTIAL.
FT   DOMAIN       724    770       CYTOPLASMIC (POTENTIAL).
FT   DOMAIN        96    110       HEPARIN-BINDING (BY SIMILARITY).
FT   DOMAIN       181    188       ZINC-BINDING (BY SIMILARITY).
FT   DOMAIN       291    341       BPTI/KUNITZ INHIBITOR.
FT   DOMAIN       391    423       HEPARIN-BINDING (BY SIMILARITY).
FT   DOMAIN       491    522       HEPARIN-BINDING (BY SIMILARITY).
FT   DOMAIN       523    540       COLLAGEN-BINDING (BY SIMILARITY).
FT   DOMAIN       732    751       INTERACTION WITH G(O)-ALPHA
FT                                  (BY SIMILARITY).
FT   DOMAIN       230    260       ASP/GLU-RICH (ACIDIC).
FT   DOMAIN       274    280       POLY-THR.
FT   SITE         144    144       REQUIRED FOR COPPER(II) REDUCTION
FT                                  (BY SIMILARITY).
FT   ACT_SITE     301    302       REACTIVE BOND (BY SIMILARITY).
FT   SITE         671    672       CLEAVAGE (BY BETA-SECRETASE)
FT                                  (BY SIMILARITY).
FT   SITE         672    673       CLEAVAGE (BY CASPASE-6) (BY SIMILARITY).
FT   SITE         687    688       CLEAVAGE (BY ALPHA-SECRETASE)
FT                                  (BY SIMILARITY).
FT   SITE         704    704       IMPLICATED IN FREE RADICAL PROPAGATION
FT                                  (BY SIMILARITY).
FT   SITE         706    706       INVOLVED IN OXIDATIVE REACTIONS
FT                                  (BY SIMILARITY).
FT   SITE         711    712       CLEAVAGE (BY GAMMA-SECRETASE; SITE 1)
FT                                  (BY SIMILARITY).
FT   SITE         713    714       CLEAVAGE (BY GAMMA-SECRETASE; SITE 2)
FT                                  (BY SIMILARITY).
FT   SITE         720    721       CLEAVAGE (BY GAMMA-SECRETASE; SITE 3)
FT                                  (BY SIMILARITY).
FT   SITE         724    734       BASOLATERAL SORTING SIGNAL
FT                                  (BY SIMILARITY).
FT   SITE         739    740       CLEAVAGE (BY CASPASES-3,-6,-8 OR -9)
FT                                  (BY SIMILARITY).
FT   SITE         757    760       ENDOCYTOSIS SIGNAL.
FT   SITE         759    762       NPXY MOTIF.

  Query Match             100.0%;  Score 40;  DB 1;  Length 770;
  Best Local Similarity   100.0%;  Pred. No. 0.61;
  Matches    8;  Conservative    0;  Mismatches    0;  Indels    0;  Gaps    0;

Qy          1 EVKMDAEF 8
              ||||||||
Db        668 EVKMDAEF 675


RESULT 10
A4_MOUSE
ID   A4_MOUSE       STANDARD;      PRT;   770 AA.
AC   P12023; P97487; P97942; Q99K32;
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DT   01-OCT-1989 (Rel. 12, Created)
DT   15-SEP-2003 (Rel. 42, Last sequence update)
DT   15-SEP-2003 (Rel. 42, Last annotation update)
DE   Amyloid beta A4 protein precursor (APP) (ABPP) (Alzheimer's disease
DE   amyloid protein homolog) (Amyloidogenic glycoprotein) (AG) [Contains:
DE   Soluble APP-alpha (S-APP-alpha); Soluble APP-beta (S-APP-beta); C99
DE   (APP-C99); Beta-amyloid protein 42 (Beta-APP42); Beta-amyloid protein
DE   40 (Beta-APP40); C83; P3(42); P3(40); Gamma-CTF(59) (Gamma-secretase
DE   C-terminal fragment 59) (Amyloid intracellular domain 59) (AID(59))
DE   (APP-C59); Gamma-CTF(57) (Gamma-secretase C-terminal fragment 57)
DE   (Amyloid intracellular domain 57) (AID(57)) (APP-C57); Gamma-CTF(50)
DE   (Gamma-secretase C-terminal fragment 50) (Amyloid intracellular domain
DE   50) (AID(50)); C31].
GN   APP.
OS   Mus musculus (Mouse).
OC   Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
OC   Mammalia; Eutheria; Rodentia; Sciurognathi; Muridae; Murinae; Mus.
OX   NCBI_TaxID=10090;
RN   [1]
RP   SEQUENCE FROM N.A. (ISOFORM APP695).
RC   TISSUE=Brain;
RX   MEDLINE=88106489; PubMed=3322280;
RA   Yamada T., Sasaki H., Furuya H., Miyata T., Goto I., Sakaki Y.;
RT   "Complementary DNA for the mouse homolog of the human amyloid beta
RT   protein precursor.";
RL   Biochem. Biophys. Res. Commun. 149:665-671(1987).
RN   [2]
RP   REVISIONS.
RA   Yamada T.;
RL   Submitted (MAR-1988) to the EMBL/GenBank/DDBJ databases.
RN   [3]
RP   SEQUENCE FROM N.A. (ISOFORM APP695).
RC   STRAIN=BALB/c; TISSUE=Brain;
RX   MEDLINE=92096458; PubMed=1756177;
RA   de Strooper B., van Leuven F., van den Berghe H.;
RT   "The amyloid beta protein precursor or proteinase nexin II from mouse
RT   is closer related to its human homolog than previously reported.";
RL   Biochim. Biophys. Acta 1129:141-143(1991).
RN   [4]
RP   SEQUENCE FROM N.A. (ISOFORM APP695).
RC   STRAIN=SAMP8; TISSUE=Hippocampus;
RX   PubMed=11235921;
RA   Kumar V.B., Vyas K., Franko M., Choudhary V., Buddhiraju C.,
RA   Alvarez J., Morley J.E.;
RT   "Molecular cloning, expression, and regulation of hippocampal amyloid
RT   precursor protein of senescence accelerated mouse (SAMP8).";
RL   Biochem. Cell Biol. 79:57-67(2001).
RN   [5]
RP   SEQUENCE OF 1-19 FROM N.A.
RX   MEDLINE=92209998; PubMed=1555768;
RA   Izumi R., Yamada T., Yoshikai S.I., Sasaki H., Hattori M.,
RA   Sakai Y.;
RT   "Positive and negative regulatory elements for the expression of the
RT   Alzheimer's disease amyloid precursor-encoding gene in mouse.";
RL   Gene 112:189-195(1992).
RN   [6]
RP   PARTIAL SEQUENCE FROM N.A. (ISOFORM APP770).
```

RC TISSUE=Breast tumor;
RX MEDLINE=22388257; PubMed=12477932;
RA Strausberg R.L., Feingold E.A., Grouse L.H., Derge J.G.,
RA Klausner R.D., Collins F.S., Wagner L., Shenmen C.M., Schuler G.D.,
RA Altschul S.F., Zeeberg B., Buetow K.H., Schaefer C.F., Bhat N.K.,
RA Hopkins R.F., Jordan H., Moore T., Max S.I., Wang J., Hsieh F.,
RA Diatchenko L., Marusina K., Farmer A.A., Rubin G.M., Hong L.,
RA Stapleton M., Soares M.B., Bonaldo M.F., Casavant T.L., Scheetz T.E.,
RA Brownstein M.J., Usdin T.B., Toshiyuki S., Carninci P., Prange C.,
RA Raha S.S., Loquellano N.A., Peters G.J., Abramson R.D., Mullahy S.J.,
RA Bosak S.A., McEwan P.J., McKernan K.J., Malek J.A., Gunaratne P.H.,
RA Richards S., Worley K.C., Hale S., Garcia A.M., Gay L.J., Hulyk S.W.,
RA Villalon D.K., Muzny D.M., Sodergren E.J., Lu X., Gibbs R.A.,
RA Fahey J., Helton E., Ketteman M., Madan A., Rodrigues S., Sanchez A.,
RA Whiting M., Madan A., Young A.C., Shevchenko Y., Bouffard G.G.,
RA Blakesley R.W., Touchman J.W., Green E.D., Dickson M.C.,
RA Rodriguez A.C., Grimwood J., Schmutz J., Myers R.M.,
RA Butterfield Y.S.N., Krzywinski M.I., Skalska U., Smailus D.E.,
RA Schnerch A., Schein J.E., Jones S.J.M., Marra M.A.;
RT "Generation and initial analysis of more than 15,000 full-length human
RT and mouse cDNA sequences.";
RL Proc. Natl. Acad. Sci. U.S.A. 99:16899-16903(2002).
RN [7]
RP SEQUENCE OF 281-380 FROM N.A., AND ALTERNATIVE SPLICING.
RC TISSUE=Brain, and Kidney;
RX MEDLINE=89149813; PubMed=2493250;
RA Yamada T., Sasaki H., Dohura K., Goto I., Sakaki Y.;
RT "Structure and expression of the alternatively-spliced forms of mRNA
RT for the mouse homolog of Alzheimer's disease amyloid beta protein
RT precursor.";
RL Biochem. Biophys. Res. Commun. 158:906-912(1989).
RN [8]
RP SEQUENCE OF 289-364 FROM N.A.
RC STRAIN=CD-1; TISSUE=Placenta;
RX MEDLINE=89345111; PubMed=2569710;
RA Fukuchi K., Martin G.M., Deeb S.S.;
RT "Sequence of the protease inhibitor domain of the A4 amyloid protein
RT precursor of Mus domesticus.";
RL Nucleic Acids Res. 17:5396-5396(1989).
RN [9]
RP SEQUENCE OF 656-737 FROM N.A.
RC STRAIN=129/Sv;
RA Wragg M.A., Busfield F., Duff K., Korenblat K., Capecchi M.,
RA Loring J.F., Goate A.M.;
RT "Introduction of six mutations into the mouse genome using 'Hit and
RT Run' gene-targeting: introduction of familial Alzheimer's disease
RT mutations into the mouse amyloid precursor protein gene and
RT humanization of the A-beta fragment.";
RL Submitted (DEC-1996) to the EMBL/GenBank/DDBJ databases.
RN [10]
RP TISSUE SPECIFICITY OF ALTERNATIVE SPLICED FORMS.
RX PubMed=8510506;
RA Sola C., Mengod G., Ghetti B., Palacios J.M., Triarhou L.C.;
RT "Regional distribution of the alternatively spliced isoforms of beta
RT APP RNA transcript in the brain of normal, heterozygous and
RT homozygous weaver mutant mice as revealed by in situ hybridization
RT histochemistry.";

RL Brain Res. Mol. Brain Res. 17:340-346(1993).
RN [11]
RP INTERACTION WITH KNS2.
RX PubMed=11144355;
RA Kamal A., Stokin G.B., Yang Z., Xia C.-H., Goldstein L.S.;
RT "Axonal transport of amyloid precursor protein is mediated by direct
RT binding to the kinesin light chain subunit of kinesin-I.";
RL Neuron 28:449-459(2000).
RN [12]
RP C-TERMINAL PROTEIN-PROTEIN INTERACTIONS, AND MUTAGENESIS OF TYR-728;
RP THR-743; TYR-757; ASN-759 AND TYR-762.
RX MEDLINE=21408156; PubMed=11517249;
RA Matsuda S., Yasukawa T., Homma Y., Ito Y., Niikura T., Hiraki T.,
RA Hirai S., Ohno S., Kita Y., Kawasumi M., Kouyama K., Yamamoto T.,
RA Kyriakis J.M., Nishimoto I.;
RT "C-jun N-terminal kinase (JNK)-interacting protein-1b/islet-brain-1
RT scaffolds Alzheimer's amyloid precursor protein with JNK.";
RL J. Neurosci. 21:6597-6607(2001).
RN [13]
RP INTERACTION WITH MAPK8IP1, AND PHOSPHORYLATION.
RX MEDLINE=22028091; PubMed=11912189;
RA Taru H., Iijima K.-I., Hase M., Kirino Y., Yagi Y., Suzuki T.;
RT "Interaction of Alzheimer's beta-amyloid precursor family proteins
RT with scaffold proteins of the JNK signaling cascade.";
RL J. Biol. Chem. 277:20070-20078(2002).
RN [14]
RP INTERACTION OF CTF PEPTIDES WITH NUMB.
RX PubMed=12011466;
RA Roncarati R., Sestan N., Scheinfeld M.H., Berechid B.E., Lopez P.A.,
RA Meucci O., McGlade J.C., Rakic P., D'Adamio L.;
RT "The gamma-secretase-generated intracellular domain of beta-amyloid
RT precursor protein binds Numb and inhibits Notch signaling.";
RL Proc. Natl. Acad. Sci. U.S.A. 99:7102-7107(2002).
RN [15]
RP GAMMA-SECRETASE PROCESSING, AND INTERACTION WITH APBB1.
RX PubMed=11553691;
RA Cupers P., Orlans I., Craessaerts K., Annaert W., De Strooper B.;
RT "The amyloid precursor protein (APP)-cytoplasmic fragment generated by
RT gamma-secretase is rapidly degraded but distributes partially in a
RT nuclear fraction of neurones in culture.";
RL J. Neurochem. 78:1168-1178(2001).
CC -!- FUNCTION: Functions as a cell surface receptor and performs
CC physiological functions on the surface of neurons relevant to
CC neurite growth, neuronal adhesion and axonogenesis. Involved in
CC cell mobility and transcription regulation through protein-protein
CC interactions. Can promote transcription activation through binding
CC to APBB1/Tip60 and inhibit Notch signaling through interaction
CC with Numb. Couples to apoptosis-inducing pathways such as those
CC mediated by G(O) and JIP. Inhibits G(O) alpha ATPase activity (By
CC similarity). Acts as a kinesin I membrane receptor, mediating the
CC axonal transport of beta-secretase and presenilin 1. May be
CC involved in copper homeostasis/oxidative stress through copper ion
CC reduction. Can regulate neurite outgrowth through binding to
CC components of the extracellular matrix such as heparin and
CC collagen I and IV (By similarity). The splice isoforms that
CC contain the BPTI domain possess protease inhibitor activity (By
CC similarity).

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CC   -!- FUNCTION: Beta-amyloid peptides are lipophilic metal chelators
CC       with metal-reducing activity. Bind transient metals such as
CC       copper, zinc and iron. Rat and mouse beta-amyloid peptides bind
CC       only weakly transient metals and have little reducing activity due
CC       to substitutions of transient metal chelating residues. Beta-APP42
CC       may activate mononuclear phagocytes in the brain and elicit
CC       inflammatory responses. Promotes both tau aggregation and TPK II-
CC       mediated phosphorylation (By similarity).
CC   -!- FUNCTION: The gamma-CTF peptides as well as the caspase-cleaved
CC       peptides, including C31, are potent enhancers of neuronal
CC       apoptosis.
CC   -!- SUBUNIT: Binds, via its C-terminal, to the PID domain of several
CC       cytoplasmic proteins, including APBB family members, the APBA
CC       family, MAPK8IP1, SHC1, Numb and Dab1. Binding to Dab1 inhibits
CC       its serine phosphorylation. Also interacts with GPCR-like protein
CC       BPP, FPRL1, APPBP1, IB1, KNS2 (via its TPR domains), APPBP2 (via
CC       BaSS) and DDB1 (By similarity). In vitro, it binds MAPT via the
CC       MT-binding domains (By similarity). Associates with microtubules
CC       in the presence of ATP and in a kinesin-dependent manner (By
CC       similarity). Interacts, through a C-terminal domain, with GNAO1
CC       (By similarity). Amyloid beta-42 binds CHRNA7 in hippocampal
CC       neurons (By similarity). Beta-amyloid associates with HADH2 (By
CC       similarity).
CC   -!- SUBCELLULAR LOCATION: Type I membrane protein. Cell surface
CC       protein that rapidly becomes internalized via clatherin-coated
CC       pits. During maturation, the immature APP (N-glycosylated in the
CC       endoplasmic reticulum) moves to the Golgi complex where complete

  Query Match             100.0%;  Score 40;  DB 1;  Length 770;
  Best Local Similarity   100.0%;  Pred. No. 0.61;
  Matches    8;  Conservative    0;  Mismatches    0;  Indels    0;  Gaps    0;

Qy          1 EVKMDAEF 8
              ||||||||
Db        668 EVKMDAEF 675


RESULT 11
A4_PIG
ID   A4_PIG          STANDARD;      PRT;   770 AA.
AC   P79307; Q29023; Q9TUI0;
DT   01-NOV-1997 (Rel. 35, Created)
DT   15-SEP-2003 (Rel. 42, Last sequence update)
DT   15-SEP-2003 (Rel. 42, Last annotation update)
DE   Amyloid beta A4 protein precursor (APP) (ABPP) (Alzheimer's disease
DE   amyloid protein homolog) [Contains: Soluble APP-alpha (S-APP-alpha);
DE   Soluble APP-beta (S-APP-beta); C99; Beta-amyloid protein 42 (Beta-
DE   APP42); Beta-amyloid protein 40 (Beta-APP40); C83; P3(42); P3(40);
DE   Gamma-CTF(59) (Gamma-secretase C-terminal fragment 59); Gamma-CTF(57)
DE   (Gamma-secretase C-terminal fragment 57); Gamma-CTF(50) (Gamma-
DE   secretase C-terminal fragment 50); C31].
OS   Sus scrofa (Pig).
OC   Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
OC   Mammalia; Eutheria; Cetartiodactyla; Suina; Suidae; Sus.
OX   NCBI_TaxID=9823;
RN   [1]
RP   SEQUENCE FROM N.A.
```

RA Kimura A., Takahashi T.;
RT "Amyloid precursor protein 770.";
RL Submitted (SEP-1999) to the EMBL/GenBank/DDBJ databases.
RN [2]
RP SEQUENCE OF 1-136 FROM N.A.
RC TISSUE=Small intestine;
RA Winteroe A.K., Fredholm M.;
RT "Evaluation and characterization of a porcine small intestine cDNA
RT library.";
RL Submitted (JAN-1997) to the EMBL/GenBank/DDBJ databases.
RN [3]
RP SEQUENCE OF 667-723 FROM N.A.
RC TISSUE=Brain;
RX MEDLINE=92017079; PubMed=1656157;
RA Johnstone E.M., Chaney M.O., Norris F.H., Pascual R., Little S.P.;
RT "Conservation of the sequence of the Alzheimer's disease amyloid
RT peptide in dog, polar bear and five other mammals by cross-species
RT polymerase chain reaction analysis.";
RL Brain Res. Mol. Brain Res. 10:299-305(1991).
CC -!- FUNCTION: Functions as a cell surface receptor and performs
CC physiological functions on the surface of neurons relevant to
CC neurite growth, neuronal adhesion and axonogenesis. Involved in
CC cell mobility and transcription regulation through protein-protein
CC interactions (By similarity). Can promote transcription activation
CC through binding to APBB1/Tip60 and inhibit Notch signaling through
CC interaction with Numb (By similarity). Couples to apoptosis-
CC inducing pathways such as those mediated by G(O) and JIP (By
CC similarity). Inhibits G(0) alpha ATPase activity (By similarity).
CC Acts as a kinesin I membrane receptor, mediating the axonal
CC transport of beta-secretase and presenilin 1 (By similarity). May
CC be involved in copper homeostasis/oxidative stress through copper
CC ion reduction (By similarity). In vitro, copper-metallated APP
CC induces neuronal death directly or is potentiated through Cu(II)-
CC mediated low-density lipoprotein oxidation (By similarity). Can
CC regulate neurite outgrowth through binding to components of the
CC extracellular matrix such as heparin and collagen I and IV (By
CC similarity).
CC -!- FUNCTION: Beta-amyloid peptides are lipophilic metal chelators
CC with metal-reducing activity. Bind transient metals such as
CC copper, zinc and iron (By similarity).
CC -!- FUNCTION: The gamma-CTF peptides as well as the caspase-cleaved
CC peptides, including C31, are potent enhancers of neuronal
CC apoptosis (By similarity).
CC -!- SUBUNIT: Binds, via its C-terminal, to the PID domain of several
CC cytoplasmic proteins, including APBB family members, the APBA
CC family, MAPK8IP1, and SHC1, Numb and Dab1 (By similarity). Binding
CC to Dab1 inhibits its serine phosphorylation (By similarity). Also
CC interacts with GPCR-like protein BPP, FPRL1, APPBP1, IB1, KNS2
CC (via its TPR domains) (By similarity), APPBP2 (via BaSS) and DDB1.
CC In vitro, it binds MAPT via the MT-binding domains (By
CC similarity). Associates with microtubules in the presence of ATP
CC and in a kinesin-dependent manner (By similarity).
CC -!- SUBCELLULAR LOCATION: Type I membrane protein. Cell surface
CC protein that rapidly becomes internalized via clatherin-coated
CC pits. During maturation, the immature APP (N-glycosylated in the
CC endoplasmic reticulum) moves to the Golgi complex where complete
CC maturation occurs (O-glycosylated and sulfated). After alpha-

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CC       secretase cleavage, soluble APP is released into the extracellular
CC       space and the C-terminal is internalized to endosomes and
CC       lysosomes. Some APP accumulates in secretory transport vesicles
CC       leaving the late Golgi compartment and returns to the cell
CC       surface. GammaCTF(59) peptide is located to both the cytoplasm and
CC       nuclei of neurons (By similarity).
CC   -!- DOMAIN: The basolateral sorting signal (BaSS) is required for
CC       sorting of membrane proteins to the basolateral surface of
CC       epithelial cells (By similarity).
CC   -!- DOMAIN: The NPXY sequence motif found in many tyrosine-
CC       phosphorylated proteins is required for the specific binding of
CC       the PID domain. However additional amino acids either N- or C-
CC       terminal to the NPXY motif are often required for complete
CC       interaction. The PID domain-containing proteins which bind APP
CC       require the YENPTY motif for full interaction. These interactions
CC       are independent of phosphorylation on the terminal tyrosine
CC       residue. The NPXY site is also involved in clatherin-mediated
CC       endocytosis (By similarity).
CC   -!- PTM: Proteolytically processed under normal cellular conditions.
CC       Cleavage by alpha-secretase or alternatively by beta-secretase
CC       leads to generation and extracellular release of soluble APP
CC       peptides, S-APP-alpha and S-APP-beta, respectively, and the
CC       retention of corresponding membrane-anchored C-terminal fragments,
CC       C83 and C99. Subsequent processing of C83 by gamma-secretase
CC       yields P3 peptides. This is the major secretory pathway and is
CC       nonamyloidogenic. Alternatively, presenilin/nicastrin-mediated
CC       gamma-secretase processing of C99 releases the amyloid beta
CC       proteins, amyloid-beta 40 (Abeta40) and amyloid-beta 42 (Abeta42),
CC       major components of amyloid plaques, and the cytotoxic C-terminal
CC       fragments, gammaCTF(50), gammaCTF(57) and gammaCTF(59) (By
CC       similarity).
CC   -!- PTM: Proteolytically cleaved by caspases during neuronal apoptosis
CC       (By similarity). Cleavage at Asp-739 by either caspase-3, -8 or -9
CC       results in the production of the neurotoxic C31 peptide and the
CC       increased production of beta-amyloid peptides (By similarity).
CC   -!- PTM: N- and O-linked glycosylated (By similarity).
CC   -!- PTM: Phosphorylation in the C-terminal on tyrosine, threonine and
CC       serine residues is neuron-specific. Phosphorylation can affect APP
CC       processing, neuronal differentiation and interaction with other
CC       proteins (By similarity).
CC   -!- PTM: Extracellular binding and reduction of copper, results in a
CC       corresponding oxidation of Cys-144 and Cys-158, and the formation
CC       of a disulfide bond (By similarity).
CC   -!- MISCELLANEOUS: Chelation of metal ions, notably copper, iron and
CC       zinc, can induce histidine-bridging between beta-amyloid molecules
CC       resulting in beta-amyloid-metal aggregates (By similarity).
CC       Extracellular zinc-binding increases binding of heparin to APP and
CC       inhibits collagen-binding (By similarity).
CC   -!- SIMILARITY: BELONGS TO THE APP FAMILY.
CC   -!- SIMILARITY: Contains 1 BPTI/Kunitz inhibitor domain.
CC   ----------------------------------------------------------------------
CC   This SWISS-PROT entry is copyright. It is produced through a collaboration
CC   between the Swiss Institute of Bioinformatics and the EMBL outstation -
CC   the European Bioinformatics Institute. There are no restrictions on its
CC   use by non-profit institutions as long as its content is in no way
CC   modified and this statement is not removed. Usage by and for commercial
CC   entities requires a license agreement (See http://www.isb-sib.ch/announce/
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CC   or send an email to license@isb-sib.ch).
CC   -----------------------------------------------------------------------
DR   EMBL; AB032550; BAA84580.1; -.
DR   EMBL; Z84022; CAB06313.1; -.
DR   EMBL; X56127; CAA39592.1; -.
DR   HSSP; P05067; 1AAP.
DR   InterPro; IPR008155; A4_APP.
DR   InterPro; IPR008154; A4_extra.
DR   InterPro; IPR001255; Beta-APP.
DR   InterPro; IPR002223; Kunitz_BPTI.
DR   Pfam; PF02177; A4_EXTRA; 1.
DR   PRINTS; PR00203; AMYLOIDA4.
DR   PRINTS; PR00759; BASICPTASE.
DR   ProDom; PD000222; Kunitz_BPTI; 1.
DR   SMART; SM00006; A4_EXTRA; 1.
DR   SMART; SM00131; KU; 1.
DR   PROSITE; PS00319; A4_EXTRA; 1.
DR   PROSITE; PS00320; A4_INTRA; 1.
DR   PROSITE; PS00280; BPTI_KUNITZ_1; 1.
DR   PROSITE; PS50279; BPTI_KUNITZ_2; 1.
KW   Apoptosis; Endocytosis; Cell adhesion; Serine protease inhibitor;
KW   Coated pits; Neurone; Heparin-binding; Metal-binding; Copper; Iron;
KW   Zinc; Signal; Transmembrane; Glycoprotein; Phosphorylation;
KW   Amyloid.
FT   SIGNAL        1     17       BY SIMILARITY.
FT   CHAIN        18    770       AMYLOID BETA A4 PROTEIN.
FT   CHAIN        18    687       SOLUBLE APP-ALPHA (POTENTIAL).
FT   CHAIN        18    671       SOLUBLE APP-BETA (POTENTIAL).
FT   CHAIN       672    770       C99 (BY SIMILARITY).
FT   CHAIN       672    713       BETA-AMYLOID PROTEIN 42 (BY SIMILARITY).
FT   CHAIN       672    711       BETA-AMYLOID PROTEIN 40 (BY SIMILARITY).
FT   CHAIN       688    770       C83 (BY SIMILARITY).
FT   CHAIN       688    713       P3(42) (BY SIMILARITY).
FT   CHAIN       688    711       P3(40) (BY SIMILARITY).
FT   CHAIN       712    770       GAMMA-CTF(59).
FT   CHAIN       714    770       GAMMA-CTF(57).
FT   CHAIN       721    770       GAMMA-CTF(50) (BY SIMILARITY).
FT   CHAIN       740    770       C31 (DURING APOPTOSIS) (BY SIMILARITY).
FT   DOMAIN       18    699       EXTRACELLULAR (POTENTIAL).
FT   TRANSMEM    700    723       POTENTIAL.
FT   DOMAIN      724    770       CYTOPLASMIC (POTENTIAL).
FT   DOMAIN       96    110       HEPARIN-BINDING (BY SIMILARITY).
FT   DOMAIN      135    155       COPPER-BINDING (BY SIMILARITY).
FT   DOMAIN      181    188       ZINC-BINDING (BY SIMILARITY).
FT   DOMAIN      291    341       BPTI/KUNITZ INHIBITOR.
FT   DOMAIN      391    423       HEPARIN-BINDING (BY SIMILARITY).
FT   DOMAIN      491    522       HEPARIN-BINDING (BY SIMILARITY).
FT   DOMAIN      523    540       COLLAGEN-BINDING (BY SIMILARITY).
FT   DOMAIN      732    751       INTERACTION WITH G(O)-ALPHA (BY
FT                                SIMILARITY).
FT   DOMAIN      230    260       ASP/GLU-RICH (ACIDIC).
FT   DOMAIN      274    280       POLY-THR.
FT   SITE        144    144       REQUIRED FOR COPPER(II) REDUCTION
FT                                (BY SIMILARITY).
FT   ACT_SITE    301    302       REACTIVE BOND (BY SIMILARITY).
FT   SITE        671    672       CLEAVAGE (BY BETA-SECRETASE)
FT                                (BY SIMILARITY).
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FT   SITE        672    673       CLEAVAGE (BY CASPASE-6) (BY SIMILARITY).
FT   SITE        687    688       CLEAVAGE (BY ALPHA-SECRETASE)
FT                                 (BY SIMILARITY).
FT   SITE        704    704       IMPLICATED IN FREE RADICAL PROPAGATION
FT                                 (BY SIMILARITY).
FT   SITE        706    706       INVOLVED IN OXIDATIVE REACTIONS
FT                                 (BY SIMILARITY).
FT   SITE        711    712       CLEAVAGE (BY GAMMA-SECRETASE; SITE 1)
FT                                 (BY SIMILARITY).
FT   SITE        713    714       CLEAVAGE (BY GAMMA-SECRETASE; SITE 2)
FT                                 (BY SIMILARITY).

  Query Match             100.0%;  Score 40;  DB 1;  Length 770;
  Best Local Similarity   100.0%;  Pred. No. 0.61;
  Matches    8;  Conservative    0;  Mismatches    0;  Indels    0;  Gaps    0;

Qy          1 EVKMDAEF 8
              ||||||||
Db        668 EVKMDAEF 675


RESULT 12
A4_RAT
ID   A4_RAT         STANDARD;      PRT;   770 AA.
AC   P08592;
DT   01-AUG-1988 (Rel. 08, Created)
DT   01-DEC-1992 (Rel. 24, Last sequence update)
DT   15-SEP-2003 (Rel. 42, Last annotation update)
DE   Amyloid beta A4 protein precursor (APP) (Alzheimer's disease amyloid
DE   protein homolog) (Amyloidogenic glycoprotein) (AG) [Contains: Soluble
DE   APP-alpha (S-APP-alpha); Soluble APP-beta (S-APP-beta); C99; Beta-
DE   amyloid protein 42 (Beta-APP42); Beta-amyloid protein 40 (Beta-APP40);
DE   C83; P3(42); P3(40); Gamma-CTF(59) (Gamma-secretase C-terminal
DE   fragment 59); Gamma-CTF(57) (Gamma-secretase C-terminal fragment 57);
DE   Gamma-CTF(50) (Gamma-secretase C-terminal fragment 50); C31].
GN   APP.
OS   Rattus norvegicus (Rat).
OC   Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
OC   Mammalia; Eutheria; Rodentia; Sciurognathi; Muridae; Murinae; Rattus.
OX   NCBI_TaxID=10116;
RN   [1]
RP   SEQUENCE FROM N.A. (ISOFORM APP695).
RC   TISSUE=Brain;
RX   MEDLINE=88312583; PubMed=2900758;
RA   Shivers B.D., Hilbich C., Multhaup G., Salbaum J.M., Beyreuther K.,
RA   Seeburg P.H.;
RT   "Alzheimer's disease amyloidogenic glycoprotein: expression pattern
RT   in rat brain suggests a role in cell contact.";
RL   EMBO J. 7:1365-1370(1988).
RN   [2]
RP   SEQUENCE OF 289-364 FROM N.A.
RC   TISSUE=Liver;
RX   MEDLINE=89183625; PubMed=2648331;
RA   Kang J., Mueller-Hill B.;
RT   "The sequence of the two extra exons in rat preA4.";
RL   Nucleic Acids Res. 17:2130-2130(1989).
RN   [3]
```

RP SEQUENCE OF 720-730, AND MASS SPECTROMETRY.
RX PubMed=11483588;
RA Gu Y., Misonou H., Sato T., Dohmae N., Takio K., Ihara Y.;
RT "Distinct intramembrane cleavage of the beta-amyloid precursor protein
RT family resembling gamma-secretase-like cleavage of Notch.";
RL J. Biol. Chem. 276:35235-35238(2001).
RN [4]
RP ALTERNATIVE SPLICING.
RX PubMed=8624099;
RA Sandbrink R., Masters C.L., Beyreuther K.;
RT "APP gene family. Alternative splicing generates functionally related
RT isoforms.";
RL Ann. N.Y. Acad. Sci. 777:281-287(1996).
RN [5]
RP TISSUE SPECIFICITY OF APPICAN.
RX PubMed=7744833;
RA Shioi J., Pangalos M.N., Ripellino J.A., Vassilacopoulou D.,
RA Mytilineou C., Margolis R.U., Robakis N.K.;
RT "The Alzheimer amyloid precursor proteoglycan (appican) is present in
RT brain and is produced by astrocytes but not by neurons in primary
RT neural cultures.";
RL J. Biol. Chem. 270:11839-11844(1995).
RN [6]
RP TISSUE SPECIFICITY OF ISOFORMS.
RX PubMed=8996834;
RA Sandbrink R., Monning U., Masters C.L., Beyreuther K.;
RT "Expression of the APP gene family in brain cells, brain development
RT and aging.";
RL Gerontology 43:119-131(1997).
RN [7]
RP INTERACTION WITH DDB1, AND MUTAGENESIS OF TYR-757; ASN-759 AND
RP TYR-762.
RX PubMed=9930726;
RA Watanabe T., Sukegawa J., Tomita S., Iijima K.-I., Oguchi S.,
RA Suzuki T., Nairn A.C., Greengard P.;
RT "A 127-kDa protein (UV-DDB) binds to the cytoplasmic domain of the
RT Alzheimer's amyloid precursor protein.";
RL J. Neurochem. 72:549-556(1999).
RN [8]
RP INTERACTION WITH GNAO1, AND MUTAGENESIS OF HIS-732 AND HIS-733.
RX PubMed=10024358;
RA Brouillet E., Trembleau A., Galanaud D., Volovitch M., Bouillot C.,
RA Valenza C., Prochiantz A., Allinquant B.;
RT "The amyloid precursor protein interacts with Go heterotrimeric
RT protein within a cell compartment specialized in signal
RT transduction.";
RL J. Neurosci. 19:1717-1727(1999).
RN [9]
RP CHARACTERISTICS OF APPICAN, AND MUTAGENESIS OF SER-656.
RX MEDLINE=95256193; PubMed=7737970;
RA Pangalos M.N., Efthimiopoulos S., Shioi J., Robakis N.K.;
RT "The chondroitin sulfate attachment site of appican is formed by
RT splicing out exon 15 of the amyloid precursor gene.";
RL J. Biol. Chem. 270:10388-10391(1995).
RN [10]
RP BETA-AMYLOID METAL-BINDING.
RX PubMed=10386999;

RA Huang X., Atwood C.S., Hartshorn M.A., Multhaup G., Goldstein L.E.,
RA Scarpa R.C., Cuajungco M.P., Gray D.N., Lim J., Moir R.D., Tanzi R.E.,
RA Bush A.I.;
RT "The A beta peptide of Alzheimer's disease directly produces hydrogen
RT peroxide through metal ion reduction.";
RL Biochemistry 38:7609-7616(1999).
RN [11]
RP BETA-AMYLOID ZINC BINDING.
RX MEDLINE=99343552; PubMed=10413512;
RA Liu S.T., Howlett G., Barrow C.J.;
RT "Histidine-13 is a crucial residue in the zinc ion-induced aggregation
RT of the A beta peptide of Alzheimer's disease.";
RL Biochemistry 38:9373-9378(1999).
RN [12]
RP IMPORTANCE OF GLY-704 IN FREE RADICAL PROPAGATION, AND MUTAGENESIS OF
RP GLY-704.
RX PubMed=11959460;
RA Kanski J., Varadarajan S., Aksenova M., Butterfield D.A.;
RT "Role of glycine-33 and methionine-35 in Alzheimer's amyloid beta-
RT peptide 1-42-associated oxidative stress and neurotoxicity.";
RL Biochim. Biophys. Acta 1586:190-198(2001).
RN [13]
RP PHOSPHORYLATION.
RX PubMed=9085254;
RA Oishi M., Nairn A.C., Czernik A.J., Lim G.S., Isohara T., Gandy S.E.,
RA Greengard P., Suzuki T.;
RT "The cytoplasmic domain of Alzheimer's amyloid precursor protein is
RT phosphorylated at Thr654, Ser655, and Thr668 in adult rat brain and
RT cultured cells.";
RL Mol. Med. 3:111-123(1997).
RN [14]
RP PHOSPHORYLATION ON SER-730.
RX PubMed=10329382;
RA Isohara T., Horiuchi A., Watanabe T., Ando K., Czernik A.J., Uno I.,
RA Greengard P., Nairn A.C., Suzuki T.;
RT "Phosphorylation of the cytoplasmic domain of Alzheimer's beta-amyloid
RT precursor protein at Ser655 by a novel protein kinase.";
RL Biochem. Biophys. Res. Commun. 258:300-305(1999).
RN [15]
RP PHOSPHORYLATION, INDUCTION, SUBCELLULAR LOCATION, AND MUTAGENESIS OF
RP THR-743.
RX MEDLINE=99274744; PubMed=10341243;
RA Ando K., Oishi M., Takeda S., Iijima K.-I., Isohara T., Nairn A.C.,
RA Kirino Y., Greengard P., Suzuki T.;
RT "Role of phosphorylation of Alzheimer's amyloid precursor protein
RT during neuronal differentiation.";
RL J. Neurosci. 19:4421-4427(1999).
RN [16]
RP PHOSPHORYLATION ON THR-743.
RX PubMed=10936190;
RA Iijima K.-I., Ando K., Takeda S., Satoh Y., Seki T., Itohara S.,
RA Greengard P., Kirino Y., Nairn A.C., Suzuki T.;
RT "Neuron-specific phosphorylation of Alzheimer's beta-amyloid precursor
RT protein by cyclin-dependent kinase 5.";
RL J. Neurochem. 75:1085-1091(2000).
RN [17]
RP CARBOHYDRATE STRUCTURE OF APPICAN.

```
RX   PubMed=11479316;
RA   Tsuchida K., Shioi J., Yamada S., Boghosian G., Wu A., Cai H.,
RA   Sugahara K., Robakis N.K.;
RT   "Appican, the proteoglycan form of the amyloid precursor protein,
RT   contains chondroitin sulfate E in the repeating disaccharide region
RT   and 4-O-sulfated galactose in the linkage region.";
RL   J. Biol. Chem. 276:37155-37160(2001).
CC   -!- FUNCTION: Functions as a cell surface receptor and performs
CC       physiological functions on the surface of neurons relevant to
CC       neurite growth, neuronal adhesion and axonogenesis. Involved in
CC       cell mobility and transcription regulation through protein-protein
CC       interactions (By similarity). Can promote transcription activation
CC       through binding to APBB1/Tip60 and inhibit Notch signaling through
CC       interaction with Numb (By similarity). Couples to apoptosis-
CC       inducing pathways such as those mediated by G(O) and JIP. Inhibits
CC       G(O) alpha ATPase activity. Acts as a kinesin I membrane receptor,
CC       mediating the axonal transport of beta-secretase and presenilin 1
CC       (By similarity). May be involved in copper homeostasis/oxidative
CC       stress through copper ion reduction. Can regulate neurite
CC       outgrowth through binding to components of the extracellular
CC       matrix such as heparin and collagen I and IV (By similarity). The
CC       splice isoforms that contain the BPTI domain possess protease
CC       inhibitor activity (By similarity).
CC   -!- FUNCTION: Beta-amyloid peptides are lipophilic metal chelators
CC       with metal-reducing activity. Bind transient metals such as
CC       copper, zinc and iron. Rat and mouse beta-amyloid peptides bind
CC       only weakly transient metals and have little reducing activity due
CC       to substitutions of transient metal chelating residues. Beta-APP42
CC       may activate mononuclear phagocytes in the brain and elicit
CC       inflammatory responses. Promotes both tau aggregation and TPK II-
CC       mediated phosphorylation (By similarity).
CC   -!- FUNCTION: Appicans elicit adhesion of neural cells to the
CC       extracellular matrix and may regulate neurite outgrowth in the
CC       brain.
CC   -!- FUNCTION: The gamma-CTF peptides as well as the caspase-cleaved
CC       peptides, including C31, are potent enhancers of neuronal
CC       apoptosis (By similarity).
CC   -!- SUBUNIT: Binds, via its C-terminal, to the PID domain of several
CC       cytoplasmic proteins, including APBB family members, the APBA
CC       family, MAPK8IP1, SHC1 and Numb and Dab1 (By similarity). Binding
CC       to Dab1 inhibits its serine phosphorylation (By similarity). Also
CC       interacts with GPCR-like protein BPP, FPRL1, APPBP1, IB1, KNS2
CC       (via its TPR domains), APPBP2 (via BaSS) (By similarity) and DDB1.
CC       In vitro, it binds MAPT via the MT-binding domains (By
CC       similarity). Associates with microtubules in the presence of ATP
CC       and in a kinesin-dependent manner (By similarity). Interacts,
CC       through a C-terminal domain, with GNAO1. Amyloid beta-42 binds
CC       CHRNA7 in hippocampal neurons (By similarity). Beta-amyloid
CC       associates with HADH2 (By similarity).
CC   -!- SUBCELLULAR LOCATION: Type I membrane protein. Cell surface
CC       protein that rapidly becomes internalized via clatherin-coated
CC       pits. During maturation, the immature APP (N-glycosylated in the

  Query Match             100.0%;  Score 40;  DB 1;  Length 770;
  Best Local Similarity   100.0%;  Pred. No. 0.61;
  Matches    8;  Conservative    0;  Mismatches    0;  Indels    0;  Gaps    0;
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Qy          1 EVKMDAEF 8
              ||||||||
Db        668 EVKMDAEF 675


RESULT 13
BCPA_CHLLT
ID   BCPA_CHLLT     STANDARD;      PRT;   354 AA.
AC   Q46135;
DT   15-JUL-1998 (Rel. 36, Created)
DT   15-JUL-1998 (Rel. 36, Last sequence update)
DT   15-SEP-2003 (Rel. 42, Last annotation update)
DE   Bacteriochlorophyll A protein (BChl a protein) (BCP) (Fenna-Matthews-
DE   Olson protein) (FMO-protein) (Fragment).
GN   FMOA.
OS   Chlorobium limicola f.sp. thiosulfatophilum.
OC   Bacteria; Chlorobi; Chlorobia; Chlorobiales; Chlorobiaceae;
OC   Chlorobium.
OX   NCBI_TaxID=115852;
RN   [1]
RP   SEQUENCE FROM N.A.
RX   MEDLINE=95352646; PubMed=7626630;
RA   Hager-Braun C., Xie D.L., Jarosch U., Herold E., Buttner M.,
RA   Zimmermann R., Deutzmann R., Hauska G., Nelson N.;
RT   "Stable photobleaching of P840 in Chlorobium reaction center
RT   preparations: presence of the 42-kDa bacteriochlorophyll a protein
RT   and a 17-kDa polypeptide.";
RL   Biochemistry 34:9617-9624(1995).
CC   -!- FUNCTION: INTERMEDIARY IN THE TRANSFER OF EXCITATION ENERGY FROM
CC       THE CHLOROPHYLL TO THE REACTION CENTERS.
CC   -!- SUBUNIT: HOMOTRIMER. EACH SUBUNIT CONTAINS 7 MOLECULES OF
CC       BACTERIOCHLOROPHYLL A.
CC   ---------------------------------------------------------------------
CC   This SWISS-PROT entry is copyright. It is produced through a collaboration
CC   between the Swiss Institute of Bioinformatics and the EMBL outstation -
CC   the European Bioinformatics Institute. There are no restrictions on its
CC   use by non-profit institutions as long as its content is in no way
CC   modified and this statement is not removed. Usage by and for commercial
CC   entities requires a license agreement (See http://www.isb-sib.ch/announce/
CC   or send an email to license@isb-sib.ch).
CC   ---------------------------------------------------------------------
DR   EMBL; X83529; CAA58510.1; -.
DR   PIR; S51143; S51143.
DR   HSSP; Q46393; 1KSA.
DR   InterPro; IPR003426; BChl_A.
DR   Pfam; PF02327; BChl_A; 1.
DR   ProDom; PD041784; BChl_A; 1.
KW   Electron transport; Photosynthesis; Reaction center; Magnesium;
KW   Bacteriochlorophyll.
FT   NON_TER       1      1
FT   METAL        99     99       MAGNESIUM (BACTERIOCHLOROPHYLL A 1 AXIAL
FT                                LIGAND) (BY SIMILARITY).
FT   METAL       134    134       MAGNESIUM (BACTERIOCHLOROPHYLL A 6 AXIAL
FT                                LIGAND) (BY SIMILARITY).
FT   METAL       278    278       MAGNESIUM (BACTERIOCHLOROPHYLL A 4 AXIAL
FT                                LIGAND) (BY SIMILARITY).
FT   METAL       285    285       MAGNESIUM (BACTERIOCHLOROPHYLL A 7 AXIAL
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FT                                   LIGAND) (BY SIMILARITY).
FT   METAL       286    286          MAGNESIUM (BACTERIOCHLOROPHYLL A 3 AXIAL
FT                                   LIGAND) (BY SIMILARITY).
SQ   SEQUENCE   354 AA;  39243 MW;  F4D4D565BDDCDB1B CRC64;

  Query Match             80.0%;  Score 32;  DB 1;  Length 354;
  Best Local Similarity   75.0%;  Pred. No. 15;
  Matches    6;  Conservative    1;  Mismatches    1;  Indels    0;  Gaps    0;

Qy          1 EVKMDAEF 8
              |||:| ||
Db        254 EVKVDGEF 261


RESULT 14
BCPA_CHLTE
ID   BCPA_CHLTE     STANDARD;      PRT;   365 AA.
AC   Q46393;
DT   15-JUL-1998 (Rel. 36, Created)
DT   15-JUL-1998 (Rel. 36, Last sequence update)
DT   15-SEP-2003 (Rel. 42, Last annotation update)
DE   Bacteriochlorophyll A protein (BChl a protein) (BCP) (Fenna-Matthews-
DE   Olson protein) (FMO-protein).
GN   FMOA OR CT1499.
OS   Chlorobium tepidum.
OC   Bacteria; Chlorobi; Chlorobia; Chlorobiales; Chlorobiaceae;
OC   Chlorobium.
OX   NCBI_TaxID=1097;
RN   [1]
RP   SEQUENCE FROM N.A.
RA   Dracheva S., Williams J.A.C., Blankenship R.E.;
RT   "Cloning and sequencing of the FMO-protein gene from Chlorobium
RT   tepidum.";
RL   (In) Murata N. (eds.);
RL   Research in photosynthesis, pp.2:53-56, Kluwer Academic Publishers,
RL   Dordrecht (1992).
RN   [2]
RP   SEQUENCE FROM N.A.
RC   STRAIN=TLS / ATCC 49652 / DSM 12025;
RX   MEDLINE=22103685; PubMed=12093901;
RA   Eisen J.A., Nelson K.E., Paulsen I.T., Heidelberg J.F., Wu M.,
RA   Dodson R.J., Deboy R., Gwinn M.L., Nelson W.C., Haft D.H.,
RA   Hickey E.K., Peterson J.D., Durkin A.S., Kolonay J.L., Yang F.,
RA   Holt I., Umayam L.A., Mason T., Brenner M., Shea T.P., Parksey D.,
RA   Nierman W.C., Feldblyum T.V., Hansen C.L., Craven M.B., Radune D.,
RA   Vamathevan J., Khouri H., White O., Gruber T.M., Ketchum K.A.,
RA   Venter J.C., Tettelin H., Bryant D.A., Fraser C.M.;
RT   "The complete genome sequence of Chlorobium tepidum TLS, a
RT   photosynthetic, anaerobic, green-sulfur bacterium.";
RL   Proc. Natl. Acad. Sci. U.S.A. 99:9509-9514(2002).
RN   [3]
RP   X-RAY CRYSTALLOGRAPHY (2.5 ANGSTROMS).
RX   MEDLINE=97415773; PubMed=9268671;
RA   Li Y.F., Zhou W., Blankenship R.E., Allen J.P.;
RT   "Crystal structure of the bacteriochlorophyll a protein from
RT   Chlorobium tepidum.";
RL   J. Mol. Biol. 271:456-471(1997).
```

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CC   -!- FUNCTION: INTERMEDIARY IN THE TRANSFER OF EXCITATION ENERGY FROM
CC       THE CHLOROPHYLL TO THE REACTION CENTERS.
CC   -!- SUBUNIT: HOMOTRIMER. EACH SUBUNIT CONTAINS 7 MOLECULES OF
CC       BACTERIOCHLOROPHYLL A.
CC   ---------------------------------------------------------------------
CC   This SWISS-PROT entry is copyright. It is produced through a collaboration
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CC   use by non-profit institutions as long as its content is in no way
CC   modified and this statement is not removed. Usage by and for commercial
CC   entities requires a license agreement (See http://www.isb-sib.ch/announce/
CC   or send an email to license@isb-sib.ch).
CC   ---------------------------------------------------------------------
DR   EMBL; L13700; AAA23111.1; -.
DR   EMBL; AE012906; AAM72726.1; -.
DR   PDB; 1KSA; 25-FEB-98.
DR   PDB; 1M50; 25-FEB-03.
DR   TIGR; CT1499; -.
DR   InterPro; IPR003426; BChl_A.
DR   Pfam; PF02327; BChl_A; 1.
DR   ProDom; PD041784; BChl_A; 1.
KW   Electron transport; Photosynthesis; Reaction center; Magnesium;
KW   3D-structure; Bacteriochlorophyll; Complete proteome.
FT   INIT_MET      0      0       BY SIMILARITY.
FT   METAL       110    110       MAGNESIUM (BACTERIOCHLOROPHYLL A 1 AXIAL
FT                                LIGAND).
FT   METAL       145    145       MAGNESIUM (BACTERIOCHLOROPHYLL A 6 AXIAL
FT                                LIGAND).
FT   METAL       289    289       MAGNESIUM (BACTERIOCHLOROPHYLL A 4 AXIAL
FT                                LIGAND).
FT   METAL       296    296       MAGNESIUM (BACTERIOCHLOROPHYLL A 7 AXIAL
FT                                LIGAND).
FT   METAL       297    297       MAGNESIUM (BACTERIOCHLOROPHYLL A 3 AXIAL
FT                                LIGAND).
FT   STRAND       11     19
FT   STRAND       27     33
FT   STRAND       46     49
FT   STRAND       51     55
FT   STRAND       65     68
FT   STRAND       71     74
FT   TURN         75     76
FT   STRAND       77     78
FT   STRAND       81     86
FT   STRAND       89     91
FT   TURN         92     93
FT   STRAND       94     95
FT   STRAND       99    105
FT   TURN        106    107
FT   STRAND      108    109
FT   STRAND      112    122
FT   HELIX       129    132
FT   STRAND      141    152
FT   HELIX       156    167
FT   TURN        168    168
FT   HELIX       174    176
FT   TURN        177    179
FT   HELIX       180    183
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FT   TURN        186    187
FT   HELIX       188    194
FT   TURN        195    195
FT   STRAND      204    210
FT   TURN        213    214
FT   STRAND      217    222
FT   STRAND      224    228
FT   HELIX       233    236
FT   TURN        237    238
FT   HELIX       239    241
FT   TURN        245    246
FT   STRAND      251    260
FT   TURN        261    262
FT   STRAND      263    264
FT   STRAND      266    269
FT   STRAND      272    272
FT   TURN        280    281
FT   STRAND      284    284
FT   HELIX       291    297
FT   TURN        298    300
FT   STRAND      308    309
FT   STRAND      311    314
FT   TURN        318    319
FT   STRAND      321    325
FT   STRAND      332    332
FT   STRAND      337    340
FT   TURN        342    344
FT   HELIX       345    351
FT   TURN        352    354
FT   STRAND      361    365
SQ   SEQUENCE   365 AA;  40163 MW;  EB48DFF24DF6A780 CRC64;

  Query Match             80.0%;  Score 32;  DB 1;  Length 365;
  Best Local Similarity   75.0%;  Pred. No. 16;
  Matches    6;  Conservative    1;  Mismatches    1;  Indels    0;  Gaps    0;

Qy          1 EVKMDAEF 8
              |||:| ||
Db        265 EVKVDGEF 272


RESULT 15
YFA0_ANASP
ID   YFA0_ANASP     STANDARD;      PRT;  1906 AA.
AC   Q8YM40;
DT   28-FEB-2003 (Rel. 41, Created)
DT   28-FEB-2003 (Rel. 41, Last sequence update)
DT   28-FEB-2003 (Rel. 41, Last annotation update)
DE   Hypothetical protein all5100 precursor.
GN   ALL5100.
OS   Anabaena sp. (strain PCC 7120).
OC   Bacteria; Cyanobacteria; Nostocales; Nostocaceae; Nostoc.
OX   NCBI_TaxID=103690;
RN   [1]
RP   SEQUENCE FROM N.A.
RX   MEDLINE=21595285; PubMed=11759840;
RA   Kaneko T., Nakamura Y., Wolk C.P., Kuritz T., Sasamoto S.,
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RA Watanabe A., Iriguchi M., Ishikawa A., Kawashima K., Kimura T.,
RA Kishida Y., Kohara M., Matsumoto M., Matsuno A., Muraki A.,
RA Nakazaki N., Shimpo S., Sugimoto M., Takazawa M., Yamada M.,
RA Yasuda M., Tabata S.;
RT "Complete genomic sequence of the filamentous nitrogen-fixing
RT cyanobacterium Anabaena sp. strain PCC 7120.";
RL DNA Res. 8:205-213(2001).
CC -!- SIMILARITY: BELONGS TO THE UPF0192 FAMILY.
CC ---

CC ---
DR EMBL; AP003598; BAB76799.1; -.
DR PIR; AD2443; AD2443.
DR InterPro; IPR002890; A2M_N.
DR Pfam; PF01835; A2M_N; 1.
KW Hypothetical protein; Signal; Complete proteome.
FT SIGNAL 1 25 POTENTIAL.
FT CHAIN 26 1906 HYPOTHETICAL PROTEIN ALL5100.
SQ SEQUENCE 1906 AA; 211372 MW; B73C2F49C63EA92A CRC64;

Query Match 80.0%; Score 32; DB 1; Length 1906;
Best Local Similarity 75.0%; Pred. No. 79;
Matches 6; Conservative 1; Mismatches 1; Indels 0; Gaps 0;

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Qy          1 EVKMDAEF 8
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Db        736 EVKLDKEF 743
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Search completed: January 21, 2004, 09:23:07
Job time : 0.397706 secs